

THE AMERICAN SURGEON

Vol. 23, No. 1

January 1957

EXPERIENCE IN THE SURGICAL MANAGEMENT OF ATRIAL SEPTAL DEFECT AND PULMONIC STENOSIS UNDER HYPOTHERMIA

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The recent application of hypothermia technics during the operative care of selected patients has met with rather phenomenal success in many hospitals throughout the world. Hypothermia employed as an anesthetic adjunct and metabolic depressant was first applied successfully in a clinical case in November 1952 by Lewis and Taufic⁶ during the closure of an interatrial septal defect. The more recent clinical success in by-passing the heart and lungs employing a mechanical pump and "bubble" oxygenator as has been demonstrated repeatedly by Lillehei, Varco, and associates⁸ will no doubt limit the application of hypothermia to some extent, but will not entirely supplant cooling as an aid to the anesthesiologist and surgeon when confronted with some types of cardiovascular, general surgical and neurosurgical problems in which general body cooling of patients has been employed with encouraging degrees of success; e.g., rapidly performed open heart surgery during inflow and outflow occlusion; in isolated instances during operative attack on lesion of great vessels, and occasionally during the operative extirpation of neurogenic and hepatic tumors.

The direct visual and operative approach to any remedial defect or lesion is, in most hands, the method of choice for achieving the best results, provided the risk of obtaining such visualization and exposure is not unduly hazardous. It is our present belief that the simple type of atrial septal defect (ostium secundum) and isolated pulmonic stenosis, valvular or infundibular, can be most satisfactorily corrected by direct exposure under anesthesia modified by hypothermia. We wish to report on our experience in the surgical management of a small series of patients with such congenital cardiac lesions.

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ATRIAL SEPTAL DEFECTS

Atrial septal defect has in recent years been diagnosed rather frequently and is considered by most cardiologists and pediatricians as the commonest single congenital heart lesion, although Lillehei⁷ is of the considered opinion that ventricular septal defects, alone or associated with other anomalies of the heart or great vessels, as not uncommonly seen, probably exist more often than atrial septal defects.

From June 1953 to November 1955, 12 patients ranging in age from 21 months to 39 years had cardiotomy performed under hypothermia for repair of atrial septal defect by the direct method at Fitzsimons Army Hospital.

Symptomatology

A generalization has been offered by Blount² in regard to this category of congenital heart disease; he has stated as follows:

In patients above the age of 2 years, the diagnosis on clinical grounds alone is relatively easy. The diagnosis in infancy is an entirely different story. The history is of little help in the diagnosis. It is the history of any patient with a left to right shunt, and, depending upon the volume of the shunt, the symptomatology will vary.

Retarded growth, poor exercise tolerance (dyspnea without cyanosis), and frequent respiratory infections were the most common symptoms in our group of patients (table I).

Physical Findings

Evidence of physical underdevelopment was present in most of our patients, but no definite mental retardation was apparent. Bulging or undue prominence of the left anterior chest wall with heaving pulsations in this region were noted in half the patients. A thrill or shock was occasionally palpable in the pulmonic area. The heart usually was enlarged to percussion and roentgenographic examination, and a grade II, low-pitched systolic murmur was most prominent in the second left intercostal space at the left border of the sternum; the second heart sound was frequently somewhat increased and widely reduplicated at this site; a blowing pulmonic diastolic murmur was occasionally heard. A soft early dias-

TABLE I
Predominant symptoms in 12 patients with atrial septal defects

	Patients	Per Cent
Mild to severe exertional dyspnea	10	84
Retarded growth (underdeveloped)	8	66
Frequent respiratory infections	6	50
No definite symptoms	2	
Vague, indefinite (apparently unrelated symptoms), however, patient had been given digitalis . .	1	
Cardiac decompensation prior to hospitalization . .	1	

TABLE II
Common physical findings
(12 patients with atrial septal defects)

	Patients
Parasternal systolic murmur (grade II, low-pitch) best heard:	
Left 2nd intercostal space	10
Left 3rd intercostal space	1
Left 4th intercostal space	1
Associated diastolic murmur, low-pitched, blowing	3
P ₂ greater than A ₂	7
Definite physical retardation	7
Prominent left anterior chest wall (overactive cardiac pulsations)	6
Shock and/or thrill pulmonic area	5

tolic murmur at the mitral area was often heard. The systemic blood pressure was not remarkable.

Roentgenographic Findings

Fluoroscopic study usually revealed an increased vascularity of the lung fields, slight to moderate enlargement of the heart and an increase in size and amplitude of pulsation of the pulmonary artery. The right atrium often appeared vertically elongated. Expansile pulsation of hilar arteries was often seen. Roentgenograms always corroborated the fluoroscopic findings with cardiac silhouette suggesting right atrial, right ventricular and pulmonary artery enlargement. Pulmonary vascular markings were increased above normal in 10 of the 12 patients.

Electrocardiograms

Ten of the 12 patients showed a pattern of incomplete right bundle branch block on electrocardiographic tracings—a finding suggesting diastolic overloading of the right ventricle (dilatation and hypertrophy). One patient had complete right bundle branch block and one 6 year old boy had a relatively normal electrocardiogram.

Cardiac Catheterization Findings

All patients had preoperative cardiac catheterization. In most instances there was slight to moderate increase in pressures above normal in the right atrium, right ventricle and pulmonary artery. Pressure readings in millimeters of Hg in a rather typical case were as follows: Right atrium—11/5; right ventricle—42/0; pulmonary artery—44/13. Two patients had pulmonary hypertension exceeding 100 mm. Hg. All blood samples from right atria gave significantly high oxygen saturations when compared with mixed venous blood, as would be expected in left to right shunts at the atrial level. Flow ratios of pulmonic to systemic circulation ranged from 1.7:1 to 4:1. On cardiac catheterization studies, one patient was demonstrated to have, in addition to atrial septal defect, anomalous pulmonary veins entering the right atrium; the catheter entered the right atrium by way of a left superior vena cava. This patient's con-

genital defects did not lend themselves favorably to operative correction as will be mentioned later when considering the complications or difficulties occurring at surgery.

Technical Considerations

In general we have adhered to the cooling methods and technics of Swan and his associates,¹³ and are highly indebted to him for his aid and assistance during the early clinical application of hypothermia at Fitzsimons Army Hospital.

Anesthesia: Induction as a rule is accomplished with intravenous pentothal and maintained with oxygen-ether mixture after endotracheal intubation and a relaxant to prevent shivering; after desired level of cooling is obtained the patient is maintained on 100 per cent oxygen administration. A recording thermometer is placed in the rectum and electrocardiographic electrodes are attached to the extremities and connected to a cardioscope and direct writer electrocardiographic apparatus.

Cooling Method: The patient is gently placed in a tub of ice water with temperature ranging from 2-6 C. after he is sufficiently anesthetized to prevent shivering. A surgical team is immediately available at all times should ventricular fibrillation or cardiac arrest occur. A cardiologist is always present to observe the cardioscope and to serve in a consultatory capacity throughout the operative procedure. When the rectal temperature reaches 31-29 C., the patient is placed on a rubber mattress through which water of variable controlled temperature can be circulated. The cooling period usually parallels the size of the patient; the immersion time in this group of patients varied from 14 to 70 minutes—average period being 38 minutes. Temperatures always continue to drop after the patient is removed from the ice-water bath, and can be expected to drift downward an additional 3-5 C.; drifts beyond this might be expected in an occasional patient if not prevented by increase in the temperature of the water circulating in the rubber mattress on the operating table. Body temperatures ranged from 23-28 C. at the time of cardiotomy in our patients—the average being 25-27 C. which is the temperature range considered optimum for the performance of cardiotomy with inflow-outflow occlusions for periods lasting 3-8 minutes. Under hypothermia the patient's carotid pulsations are difficult to obtain or barely palpable and blood pressure is unobtainable.

Operative Procedure: Bilateral anterolateral thoracotomy is performed with division of the body of the sternum in a staggered fashion, to facilitate reapproximation; this gives adequate exposure of the heart and mediastinal structures. Usually the pleural spaces are entered through the third intercostal space on the right and the fourth on the left. The pericardium is opened widely by means of a "T" shaped incision with care not to damage the phrenic nerves; bleeding points at the severed edges of the pericardium are carefully controlled, as are all areas throughout the procedure with fine silk or cotton ties. The heart is thoroughly inspected and gently palpated to confirm the clinical diagnosis. An attempt is made to delineate the size and position of the interatrial septal defect by invaginating and palpating through the lateral wall of the dilated right

atrium. Other anomalies such as aberrant pulmonary veins, anomalous left superior vena cava, etc., are visualized and evaluated if present. The venae cavae are then isolated near the right atrium—the superior proximal to the azygos vein, and encircled with heavy cotton tape ligatures to provide the inflow occlusion during open cardiectomy.

Traction sutures are placed on the lateral wall of the right atrium to facilitate elevation for placement of a noncrushing Satinsky or Harken clamp to the atrial wall. A 3–4 cm. atriotomy incision is made in the wall isolated by the noncrushing clamp. The patient is then hyperventilated with 100 per cent oxygen for a period of 5 minutes to decrease general body carbon dioxide concentration. This creates a temporary respiratory alkalosis, as advocated by Swan¹⁴ and Scott¹⁰ for possible prevention of troublesome arrhythmias, including ventricular fibrillation. Right atrial blood samples taken immediately after this period of hyperventilation have varied from pH of 7.65 to 7.75. After occlusion of inflow channels with previously placed cotton tapes a noncrushing clamp is placed through the transverse sinus at the base of the heart and closed over the pulmonary artery and aorta. It is so placed that the aorta is occluded proximal to coronary ostia in order to prevent subsequent ingress of air into the coronary system. We do not occlude the pulmonary vessels at the root of the lungs, as the amount of blood returning to the heart from this source after pulmonary artery occlusion has not been troublesome during septal defect closure. After removal of the atrial clamp, the septal defect is visualized as blood is aspirated from the atrial compartments. A hasty digital exploration is made of the communicating atrial chambers and the mitral valve is evaluated to determine if there be any stenosis. The septal defect is again inspected to determine if it is the common secundum or the rare and more complicated and serious ostium primum type; again from the interior view of the atria the operator must determine if anomalous pulmonary veins exist.

The defect or multiple defects (cribiform type) initially were closed with interrupted figure of 8, no. 000 silk suture; our last six defects have been closed, however, with a running silk or cotton suture—one interrupted suture is placed at the superior angle or edge of the defect and after slight upward traction on this suture the continuous suture is started at the inferior angle and continued upward. Before tying this suture to the previously placed interrupted suture, the air is displaced from the left atrium by injecting saline solution through the incompletely closed defect employing a bulb syringe. Septal closure is performed meticulously to insure the patency of the ostia of the venae cavae and to avoid diverting either venous stream into the left atrium. Suture should not be placed in the anatomic location of the atrio-ventricular node and neither should the patency of the coronary sinus be compromised. If anomalous pulmonary veins exist, the septal closure should be so constructed as to divert this pulmonary venous flow into the left atrial compartment. The right atrial chamber is then filled with saline or Ringer's solution and the noncrushing clamp applied proximal to the cardiectomy incision. The superior vena cava, aorta and pulmonary artery are quickly released and the atrial incision is closed by appropriate running

suture on an atraumatic needle. It has been our policy to begin gradual release of the tape occluding the inferior vena cava 2 minutes after release of the superior vena cava; this measure was adopted to prevent rapid return of accumulated epinephrine to the heart chambers and thus possibly to decrease the likelihood of ventricular fibrillation. Recent report of animal experiments under hypothermia by Shumway and Lewis¹¹ indicating the apparent value of epinephrine to the hypothermic heart of normal dogs would seem to negate our theory regarding this possible relationship of epinephrine to ventricular fibrillation. However, we will continue to gradually release the occluded inferior vena cava to prevent sudden cardiac overdistention after correction of the congenital defect. The pericardium is loosely closed after the heart resumes a forceful beat. On three occasions hearts did not tolerate this pericardial reapproximation well; 2 patients became visibly cyanotic and troublesome arrhythmias developed; the third heart developed a complete heart block at this stage of the procedure; all 3 hearts returned to normal color and began to beat normally after release of pericardial sutures. In each instance the pericardium was more completely opened to the diaphragmatic angle and no sutures were reapplied; all 3 patients convalesced uneventfully.

Closure of the chest incision is accomplished by use of fine interrupted non-absorbable sutures after establishment of adequate pleural drainage into under water seal bottles; approximation of sternal edges is maintained with crossed stainless steel sutures. In adults a bone peg is removed from a rib and inserted into adjoining sternal marrow spaces to contribute to sternal stability and bony union.

Rewarming Patients: In our more recent cases, we have placed our patients in a warm water bath, temperature 42-44 C., for rewarming. The first 8 patients were rewarmed after cardiectomy closure by means of diathermy coils previously placed about the abdomen and pelvis. In addition, the pleural spaces were irrigated repeatedly with warm saline solution, temperature 40 C. In our hands, the warm pleural irrigation method has not been very effective and 2 patients received significant superficial burns as the result of the diathermy application; in addition, it is our opinion that those patients who had diathermy warming experienced more troublesome gastric distention and ileus than those in whom the warm water bath method was employed. No wound infections have occurred in this group of patients.

Cardiac Drug Applications: We have not recently employed prostigmine as recommended by Swan¹² since we have not been fully convinced of the merits of this agent, which he injects into the proximal portion of the temporarily clamped aorta prior to inflow and outflow occlusion. Swan and co-workers, as well as Davis and Peabody,³ are convinced that the coronary perfusion of this drug makes the cold heart less susceptible to ventricular fibrillation; they continue to report encouraging results after its use although Lewis and associates⁵ apparently have as favorable clinical results without employing prostigmine. Six of our patients had the coronary system perfused with prostigmine solution and 6 did not—3 patients in this latter group had sino-auricular node and auricu-

lar wall blockade with 1 per cent procaine solution as has been advocated by Shumacker and associates,⁹ and 3 had neither prostigmine nor procaine injection.

In the prostigmine-treated group, 1 patient developed complete heart block as the pericardium was being closed—the heart reverted to normal rhythm after the pericardial sac was widely opened. The heart of a 39 year old patient developed ventricular fibrillation early and prior to opening the pericardium (during procedure had neither prostigmine nor procaine blockade). The heart reverted to a standstill and finally to a normal rhythm after cardiac massage and injection of 4 cc. of potassium chloride solution (8 mEq) into the right ventricular chamber. This patient withstood the remainder of the septal closure well, having only auricular fibrillation which occurred at some time during operative procedures in all of our patients. One of the 3 patients who had sino-auricular nodal blockade developed ventricular fibrillation during septal repair. The chemical defibrillator (KCl solution) did not convert the heart to standstill; however, one electric

TABLE III

Complications and/or unusual findings at surgery
(12 patients with atrial septal defects)

	Patients	Per Cent
Atrial fibrillation during procedure	12	100
Ventricular fibrillation	2	17
Diathermy burn	2	17
Large, almost common atria, left superior vena cava, anomalous pulmonary veins and marked stenosis mitral valve*	1	
Anomalous right pulmonary veins opening into right atrial compartment	1	
Septum incompletely closed elsewhere—plastic button retained	1	

* This 21 year old female had marked disability due to lowered cardiac reserve. After finger fracture of the congenitally stenotic mitral valve, temporary digital pressure occlusion of septal defect caused marked cyanosis of face and upper extremities and venous pressure of over 400 mm. water; therefore, only approximately 50 per cent closure of the interatrial defect was attempted. The patient convalesced without undue complications—has since become pregnant and given birth to a normal child.

TABLE IV

Surgical data

Total inflow-outflow occlusion periods	2 minutes, 45 seconds to 6 minutes, 5 seconds (Average 4 minutes, 42 seconds)
Total operating time	2 hours, 15 minutes to 5 hours, 15 minutes (Average 3 hours, 10 minutes)
Duration of ventricular fibrillation	15 minutes (Two patients—both convalesced uneventfully) and 4 plus minutes

TABLE V
Postoperative complications

	Patients	Per Cent
Gastric distention and paralytic ileus (Controlled by naso-gastric suction)	4	33
Pulmonary congestion and atelectasis (One patient required emergency tracheotomy)	4	33
Severe tachycardia	2	17
Partial median and ulnar nerve paralysis	1	8.3
Failure to completely close defect (Postoperative cardiac catheterization confirmed)*	1	8.3
Death—40 hours after closure of septum—multiple pulmonary emboli	1	8.3

* Small residual septal defect closed at subsequent operation.

shock, $\frac{1}{10}$ second at 120 volts, gave immediate arrest and spontaneous return to a regular rhythm.

PULMONIC STENOSIS

Over a two year period, June 1953 to June 1955, 6 patients varying in age from 20 months to 23 years and suffering from valvular or infundibular pulmonic stenosis had surgical correction of these congenital defects under acutely induced hypothermia. Two of these patients had small interventricular defects in addition to pulmonary stenosis.

Electrocardiograms

Electrocardiographic studies on all 6 patients presented conclusive evidence of marked right ventricular hypertrophy.

Technical Aspects

Methods used to obtain anesthesia and hypothermia were similar to those employed for the atrial septal group of patients. Bilateral thoracic sternal tran-

TABLE VI
Predominant symptomatology
(4 patients)

	Patients	Per Cent
Exertional dyspnea (exercise tolerance reduced significantly)	4	100
Mental and/or physical retardation	4	100
Frequent pulmonary infections	2	50
Convulsive episodes	1	25
Periods of syncope	1	25
Repeated episodes of congestive failure	1	25
Cyanosis—chronic or after exertion	0	
Squatting when fatigued	0	

TABLE VII
Common physical findings
(6 patients)

	Patients	Per Cent
Harsh systolic murmur grade III-V over precordium, best heard over left 2nd or 3rd intercostal space	6	100
Chest prominence near left sternal border	6	100
Pulmonic second heart sound pure—not split	5	83
Definite cardiac enlargement	5	83
Systolic thrill pulmonic area	4	66
Definite mental and/or physical retardation	4	66
Diminished second pulmonic sound (case of infundibular stenosis)	1	17

TABLE VIII
Roentgenographic findings
(6 patients)

	Patients	Per Cent
Normal pulmonary vascular markings	5	83
Enlargement of heart		
Boot-shaped heart (enlarged to left with elevation of apex)	3	83
Generalized enlargement of cardiac silhouette	2	
Pulmonic area prominent with increased pulsation suggesting poststenotic dilatation	5	83
Pulsating hilar vessels	0	

secting incisions were made, entering the pleural spaces through the fourth intercostal space on the right side and the third on the left. The pericardium was opened widely over the right ventricle and the pulmonary artery. This myocardial exposure permits the operator to evaluate the right ventricular outflow tract for visual and palpable evidence of an infundibular stenosis. After tape ligatures are placed about the venae cavae, for subsequent inflow occlusion, the anterior surface of the proximal 3-4 cm. of the pulmonary artery which in most instances showed some degree of poststenotic dilatation is cleared of its adventitia. Traction sutures are placed in the wall of this artery and a curved or spoon Pott's ductus clamp is applied in a tangential fashion so as to only partially obstruct the pulmonary blood flow. An arterotomy 2.5-3 cm. long is then made in this portion of the artery and the patient is hyperventilated for 5 minutes prior to inflow occlusion and perfusion of the coronary system with prostigmine solution, which was employed in 5 of the 6 patients. The distal portion of the main pulmonary artery is quickly occluded with a noncrushing clamp and the Pott's clamp removed (occlusion of aorta not necessary if isolated pulmonic stenosis). An aspirating tip is employed to allow visualization of the conical (funnel type) or diaphragmatic stenotic valve which is grasped with forceps and opened widely

TABLE IX
Catheterization findings and interpretations
(6 patients)

	Right Atrial Pressure	Right Ventricular Pressure (mm. Hg)	Pulmonary Artery Pressure	Periph. Arterial Saturation	Remarks
L.A., Male, 3 yrs., 8 mos.	12/4*	160/10	—	96%	Catheter passed through a patent foramen ovale—no functioning opening thought to exist; no evidence of infundibular stenosis.
M.Y., Female, 23 yrs.	10/2*	147/8	26/9 to 23/10	94%	Considered to have pure pulmonic valvular stenosis.
S.W., Male, 21 mos.	8/-4*	116/0	—	97%	Considered to have pure pulmonic valvular stenosis.
M.A.O., Female, 3 yrs.	17/5*	87/5 to 109/6	—	—	Considered to have pure pulmonic valvular stenosis.
J.D., Male, 20 mos.	10/4*	72/14	16/10	72%	Valvular pulmonic stenosis, I.V. septal defect.
H.I.D., Female, 20 years	4/0	119/0	29/4	86%	Also small interventricular septal defect.

* Giant "A" waves recorded on RA pressure curve.

to the annulus in a transverse fashion to provide a bicuspid valve. The infundibular region is then exposed by spreading a Kelley clamp in the right ventricular outflow area or by insertion of the small finger of the operator. No evidence of infundibular stenosis was found in 5 patients. One had pure infundibular stenosis which was detected on opening the pericardium. Cardiomy was performed over the infundibular region and the infundibular wall was bitten away with punch forceps.

After intracardiac filling on release of occluding clamps and tapes and reapplication of the curved Pott's clamp to the incised artery are accomplished, the incision in pulmonary artery is closed with a running suture of arterial silk.

The hypothermic temperatures attained and methods of rewarming were comparable to those employed in the atrial septal defect series. Estimated blood loss was replaced, taking care not to over transfuse the patients.

Cardiac inflow and outflow occlusion periods ranged from 2 minutes and 10 seconds to 4 minutes in this series of patients subjected to surgical correction of right ventricular outflow obstruction—periods slightly less than the necessary occlusion periods in the septal defect group.

Complications at Surgery

Auricular fibrillation occurred at some time during heart exposure in 2 patients; no arrhythmia was present at the completion of surgical procedure and both patients convalesced uneventfully. One 21 month old patient had a minor convulsion during anesthesia induction prior to immersion cooling; pulmonic

valvulotomy was accomplished without difficulty, but the patient died 22 hours later as detailed below.

Postoperative Complications

No noteworthy or significant complications occurred in 3 patients. One patient, a 20 year old white female, suffered a cerebrovascular episode on the eighth postoperative day which was manifested by partial paralysis of the right side of the face, the right arm and right leg. The patient subsequently recovered without any apparent sequelae. One 20 month old male, whose temperature was reduced to 30 C. at surgery, did well postoperatively and was discharged on the twelfth postoperative day. On the sixteenth postoperative day "knotty lumps" were noted in the skin and subcutaneous tissues over the buttocks and abdominal panniculus. The patient was readmitted and a biopsy confirmed the diagnosis of subcutaneous fat necrosis. Over the course of several weeks the lesions showed progressive involution. This case has recently been reported by Blake and associates¹. One 21 month old male died on the first postoperative day. His temperature returned to a normal level shortly after operation; however, 6 hours later the temperature dropped to 95 F., respirations became shallow, and moderate cyanosis developed in spite of the use of oxygen by nasal catheter and oxygen tent. After rewarming the patient on a rubber mattress spasticity of his extremities and a few convulsive episodes were noted. A tracheotomy was performed in hopes of improving the obvious cerebral anoxia. The child died shortly thereafter.

Results to Date

All 5 patients have done well clinically; good to excellent improvement in symptoms have been noted. Cardiac murmurs are still present but much less harsh than before valvulotomy; a faint systolic thrill is palpable at the pulmonic area on 2 patients.

DISCUSSION

With repeated reports of acceptable mortality rates from surgical centers performing cardiac surgery with the aid of hypothermia, we are of the opinion that most cases of atrial septal defect of the ostium secundum type and cases of pure pulmonic valvular or infundibular stenosis should be corrected by direct surgical approach with good visualization in a relatively bloodless field. We believe that one would be unlikely to obtain complete closure by blind or indirect methods in the "cribiform type" of atrial septal defect as demonstrated in one of our patients who had 7 to 8 ostia scattered over the atrial septal membrane. More recently we have closed septal defects on a patient who had a large secundum type and two small openings 4-5 mm. in diameter which were situated in the rim structure of the incomplete septum; it is likely that such accessory openings would be left unclosed when indirect or blind techniques are employed. Since changing our technic to the continuous suture method of closure of septal defects we have observed no evidence of incomplete closures as was experienced

in an early case whose defect was closed with interrupted sutures. This 7 year old boy has subsequently been reoperated upon and cured.

Perfusion of oxygenated blood through the coronary system during cardiomy under hypothermia is presently being conducted experimentally by Lewis and co-workers⁵ for the prolongation of the "safe period" of inflow-outflow occlusion. In clinical cases as demonstrated with impressive success by Grow and associates⁴, this approach seems very encouraging and will no doubt extend the indications for hypothermia methods to more complicated congenital and acquired cardiac lesions.

SUMMARY

Eighteen patients, ranging in age from 20 months to 39 years, have had simple direct vision cardiomy or arteriotomy approaches for the correction of atrial septal defects or for the relief of isolated pulmonic or infundibular stenosis with the aid of acutely induced general hypothermia. Sixteen of these patients are living and follow-up studies and reports indicate that 10 who had repair of interatrial septal defects are cured and one (with additional cardiovascular defects) markedly improved. The 5 patients who had surgical relief of pulmonic stenosis have had significant to striking relief of symptoms. Three patients have been followed for over 2½ years. Two patients, one in each congenital category, failed to recover after tolerating the hypothermia and surgical procedure well. One, an adult with interatrial septal defect, developed multiple pulmonary emboli on the first postoperative day, and the other, a 21 month old infant with pure pulmonic stenosis, died approximately 20 hours after valvuloplasty from uncontrollable peripheral circulatory collapse and cerebral anoxia.

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RESECTION: A CONSERVATIVE MEASURE IN THE TREATMENT OF BONE TUMORS

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The surgeon who is called upon to treat cases of bone neoplasms is constantly striving to find a less mutilating procedure than amputation. Among the more conservative measures may be mentioned resection.

Resection may be partial, segmental or complete. An example of the latter is total scapulectomy or claviculectomy.

The indications for resection are numerous but each case must be carefully evaluated before this procedure is chosen. If, in the opinion of the surgeon, it promises a fair prospect of accomplishing complete removal of the tumor-bearing portion of the bone without unduly risking the patient's life, then it probably is justified. Function after resection should, of course, be much better than if an amputation had been chosen.

Resection is indicated in most cases of benign bone neoplasms, in many cases of borderline malignancy, and in some carefully selected cases of low grade malignant tumors. The type of tumor, its size, location, and accessibility are important factors in the decision for or against resection.

The following types of benign tumors offer opportunities for resection: osteochondroma, central chondroma, chondromyxoid fibroma, giant cell tumor and aneurismal bone cyst; also selected cases of malignant tumor including low-grade fibrosarcoma of bone, secondary chondrosarcoma, and low grade juxtacortical osteosarcoma (parosteal osteoma). Occasional cases of solitary (?) bone metastasis from renal carcinoma are suitable.

Resection is obviously indicated more frequently for benign tumors than for malignant ones. Partial resection of a bone is particularly applicable to the projecting type of osteochondroma where in suitable cases it can be applied to lesions arising in practically all of the long bones as well as the scapula and ilium.

Segmental resection with restoration of bone continuity by means of massive graft is of value in carefully selected cases of low grade fibrosarcoma, chondrosarcoma, or juxtacortical osteosarcoma, especially in the forearm bones or the humerus.

While the tendency is natural to decide upon resection rather than amputation in an ever wider range of cases, experience based on previous failures in time exerts a restraining influence and the surgeon gradually acquires the judgment that is so essential.

Failure to obtain long-term survival after resection does not necessarily mean

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Presented during the Richmond Assembly of The Southeastern Surgical Congress, March 12-15, 1956, Richmond, Virginia.



FIG. 1. Chondroma of the humerus. This case was followed for 18 years before onset of pain prompted resection.



FIG. 3. Same case. Appearance following resection with substitution of fibula. Patient is symptom free with good function 4 years later.



FIG. 2. Gross specimen of same case. One area on microscopic examination revealed chondrosarcoma.



FIG. 4. Lowgrade juxtacortical osteosarcoma. Appearance when first seen following 3 unsuccessful local attempts at removal.



FIG. 5. Resection with substitution of a massive tibial transplant to bridge the defect. Patient has a useful extremity 7 years after operation.

that the choice of procedure was unwise. If the patient develops distant metastasis but no local recurrence, it can be maintained that the choice of procedure was justified and that even if amputation had been selected the result would have been the same. However, if local recurrence does follow resection, and then an amputation is carried out with ultimate pulmonary metastasis, it may well be that with amputation performed at the outset the spread of the disease might have been prevented.

Because of the insidious behavior of tumors of cartilage origin it is urged that removal of bulky osteochondromas or central chondromas is a wise preventive measure. Moreover the histologic report of "chondroma" in cases of bulky cartilage tumors whose clinical behavior and roentgenographic appearance suggest that they are not benign should be held as suspicious and not accepted as indicating a future benign course. In the records of the Bone Tumor Department of Memorial Hospital there are many examples in support of this statement. Segmental resection of a suspected central tumor of cartilage origin, so-called enchondroma, should be performed without previous biopsy if the location of the tumor is suitable, for not infrequently the roentgenographic appearance may suggest enchondroma while the microscopic study reveals low grade chondrosarcoma. Resection of such a lesion without biopsy often results in a cure whereas if the tumor is cut into for biopsy purposes a resection thereafter is very apt to be followed by a local recurrence making amputation mandatory.



FIG. 6. Recurrent giant cell tumor with pathologic fracture



FIG. 7. Same case showing resection of tumor bearing area and substitution of a vitallium prosthesis.



FIG. 8. Chondrosarcoma of iliac bone. This case was subjected to a local resection of the involved portion of the ilium.

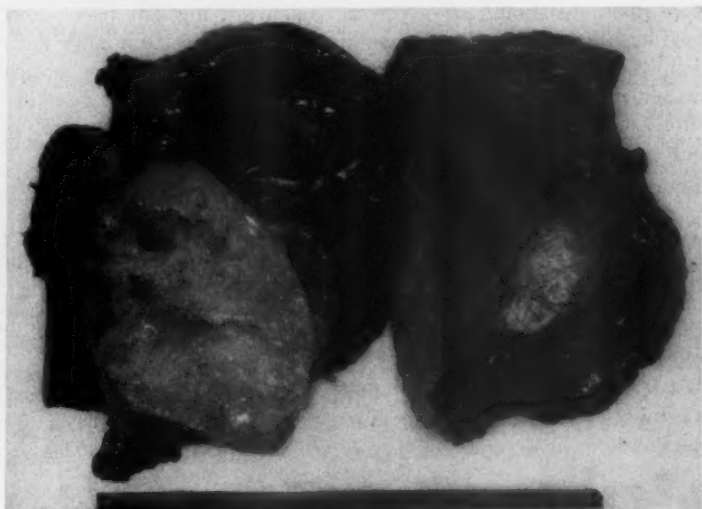


FIG. 9. Gross specimen of same case. No recurrence 3 years and 4 months after resection.

Resection of a circumscribed low grade secondary chondrosarcoma of the scapula or iliac bone is occasionally practical. Total resection of the scapula may be required for more extensive tumors and of course hemipelvectomy may be indicated by the size and location of such neoplasms in the ilium.

Low grade juxtacortical osteosarcomas of major long bones deserve at least one attempt at resection if the size and anatomic setting are suitable. If recurrence supervenes then amputation should not be deferred.

Resection has been practiced by some surgeons for highly malignant forms of bone sarcoma, *i.e.*, osteoblastic sarcoma and Ewing's sarcoma, but because of the nature of these neoplasms the results have been generally unsatisfactory. Local recurrence necessitating subsequent amputation followed by fatal metastases has been the rule. Nor should one argue in favor of a method of treatment based on a rare exceptional good result. While admitting that even early amputation fails to provide a cure in more than from 10 to 15 per cent of these very lethal sarcomas, the substitution of resection may reduce even this percentage materially and lives may be lost that otherwise might have been saved.

The employment of resection and bone graft usually is not advisable for tumors that have been subjected previously to heavy irradiation because of damage to the blood supply of the area involved which seriously interferes with wound healing and repair. If in exceptional circumstances resection and bone graft seem worthy of a trial in such heavily irradiated cases, both the patient and the surgeon should be prepared for possible failure and the need for subsequent amputation.

Technical considerations cannot be given much space in this brief communication. One point deserving of mention, however, is that there must be adequate exposure of the tumor to be resected and the adjacent normal bone. Therefore, incisions should be generous, and overlying soft parts should be mobilized even if this means extensive division of muscles; for after successful resection, the suture of divided muscles usually is followed by surprisingly satisfactory return of function. On the other hand, incomplete resection may not permit of a second conservative attempt thus making amputation obligatory.

SUMMARY

Resection as a substitute for amputation has its place in the surgical treatment of benign, borderline, and even malignant bone tumors. A careful selection of cases is required in the borderline and the frankly malignant cases. It is rarely indicated for osteoblastic sarcoma. The best results are obtained in the benign bone tumors or the low grade sarcomas of bone.

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THE PRESENT STATE OF THYROIDECTOMY

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It is our opinion, confirmed by an extensive review of the literature, that thyroidectomy is still the most useful and the most universal treatment in the handling of thyroid cases. The purpose of this paper is to try to resolve some of the ideas in the recent literature, and reach a conservative departure for decisions in the treatment of thyroid disease.

Two recent developments commanding attention are the appearance and constant improvement of the antithyroid drugs and the use, in clinical medicine, of radioactive iodine. Both have deservedly received the utmost attention from medical men and surgeons but neither has replaced surgery as a means of thyroid management. The goitrogens have now been in use as a therapeutic agent for 15 years and radioactive iodine for 14 years.^{2, 6, 7} During this time many articles have been written describing the value of each. Shades of opinion vary so much that the average physician may be easily kept in a condition of indecision as to what he had best advise his patient.⁹ As in all other decisions connected with medicine or surgery, it is reasonable to say that each case should be individualized. Still the preparation in our minds of lists of indications and contraindications make the decision regarding each individual case easier and more dependable.

Murray Franklin⁹ in a recent article made this statement: "We believe that subtotal thyroidectomy after proper medical preparation is the treatment of choice in the following types of cases of hyperthyroidism:

1. Severe primary hyperthyroidism in young adults.
2. Toxic adenomas in all age groups.
3. Recurrent hyperthyroidism following unsuccessful medical management.
4. Primary hyperthyroidism where for one reason or another, medical management is impractical.
5. Thyroid carcinoma."

He then describes somewhat at length the limitations and the indications and contraindications for the several forms of therapy.

Iodine apparently is useful in the preparation of patients with mild hyperthyroidism preoperative. X-ray treatment is used at present successfully in thyroiditis only and in the late treatment of thyroid carcinoma. Of the thiourea drugs, he favors Tapazole and Propylthiouracil and called attention to the dangers of agranulocytosis and the probability that there will be recurrence of the thyroid symptoms in 50 per cent of the patients treated. He believes that the indications for long term use are in the exophthalmic goiter in the very young and very old; recurrent postoperative hyperthyroidism; hyperthyroid patients

Presented during the Richmond Assembly of The Southeastern Surgical Congress, March 12-15, 1956, Richmond, Va.

with complications such as cardiac disease; and patients refusing operations where radioactive iodine may not be available.

It also is noteworthy that McGavack,¹³ in *Medical Clinics of North America* for 1953, refers to the work of Money and Rawson in creating tumors in small animals with the thiourea drugs. These tumors took not less than $\frac{1}{6}$ of the life span of the experimental animal to develop. This would mean in the average human being, with maximum dosage of antithyroid drugs, after 7 years fear might arise of a new growth in the thyroid as a direct result of antithyroid compounds. Rawson also believes he has seen tumor formation in the human being after a relatively short period of treatment with thiouracil. So these drugs are not without danger, especially for long term usage.

The story of radioactive iodine as used in the treatment of hyperthyroidism is no longer new. Again, shades of opinion as to its usefulness and its dangers can be found in recent articles.¹² It is obtained by prearrangement from Oak Ridge and it must be handled under conditions that have been previously arranged to protect those who handle it and those patients who receive it.¹² Considerable technical training and special care are necessary. Because of the affinity of the follicular cells for iodine,⁹ the radiation to the extent of 10,000 roentgen¹² equivalents can be conveniently given inside the thyroid with apparently no severe danger to the surrounding tissues or indeed to the distant organs.

McCullagh¹² in a recent article describes 7 characteristics that make it valuable in treatment of hyperthyroid cases. He believes that the only obstacles to its use are the difficulty in obtaining it and the fact that its effects may be blocked by iodine given in other ways, or by the thiourea drugs. He speaks from 600 odd cases and believes that it is the proper treatment for the classic Graves' disease. He believes that it may be used in high dosage with the expectation of slower effect and more frequent failure in nodular goiter. He speaks of it as the most successful isotope in medicine and thinks that it is wise to make special selection of the patients. The most pertinent indication is the recurrence of hyperthyroidism after surgery, especially is this true where there has been damage to the recurrent nerve on one side. It is also to be used in patients who are cardiac cripples or aged; and, frequently, to be used in patients who have recurrence after antithyroid drugs. Because of the fear in the minds of some of the carcinogenic properties of I-131, it seems more applicable to patients over 40 years of age but the rule is becoming more flexible as years pass.^{3, 14} So far no case of cancer in the thyroid in the human being has been attributed to radioactive iodine.^{3, 14}

It seems the consensus of opinion of those who use radioactive iodine that it had best be used in adults, preferably the older adults. A few clinics are using it in children especially in low grade dosage but it seems to be the belief this had best be done under special precautions and with long term follow-up.³ It is also definitely believed by various authors that the nodular goiter is not as effectively treated by I-131 as the diffuse toxic goiter or the classic Graves' disease.¹² Also, in the listings of several clinics, it becomes apparent that there is a belief that the exophthalmic cases,¹⁶ (those that are progressively exophthal-

mic) will best be treated first medically and then by radioactive iodine. To recapitulate then, the patients most effectively treated by I-131 are those previously subjected to thyroidectomy and with recurrence, especially those that have a nerve lesion on one side, and second, those of the older age group that have had cardiac difficulty. The more conservative observers are avoiding the treatment for children and very young people and are less inclined to use this drug in nodular goiter.³

This brings us to the consideration of the nodular goiter and the cases suspected of carcinoma. In this instance, statistics can be found to place the presence of carcinoma in the nodular goiter at 10 per cent, 12 per cent, 20 per cent, and as high as 33 per cent.¹⁶ Statistics can be found to show that the single nodule is the most dangerous.¹⁷ This appears to be true in most groups of cases that have been reported. Ochsner, however, in a recent paper, notes in his own series that the multiple nodular goiters have a slightly higher rate of malignancy than the cases with single nodules.¹⁵ Attention is called by several writers to the fact that the single nodule that has been present a long time and has begun to grow is particularly dangerous.^{11, 17} In general it is believed that the age of the patient is in direct relationship to the possibility of cure, the older patients having the best luck. In a very recent paper Todd¹⁷ after summarizing his series of 158 cases, viewing the literature on the subject, concluded as follows:

1. The incidence of malignancy in solitary nodules is high enough to warrant removal.
2. All children with nodular goiter should be considered to have carcinoma until microscopic examination of the nodule proves it is not malignant.
3. All patients with a mass in the neck adjacent to the thyroid should have excision biopsy of the lesion and further surgery at the time if microscopic study proves it to resemble thyroid tissue.
4. Toxicity in multiple nodular goiter does not mean malignancy may not be present in one of the adenomas.
5. All multiple nodular goiters should be frequently examined for possible change in size or consistency and appropriate measures taken if changes occur.
6. Radioactive iodine is of little benefit in the treatment of cancer of the thyroid except in a few isolated special cases.

Three types of carcinoma are to be found. Of these the most frequent is the papillary adenoma carcinoma and these are apparently the most readily cured by surgical removal, as metastases are often slow to the related lymph glands. Their invasiveness is somewhat limited in most cases. Varying opinion can be found for the advisability of radical or ultraradical surgical treatment. It is believed that removal of the contained lobe and the isthmus and the related glands is reasonable treatment in most cases.¹¹ Some authors add to this X-ray treatment of the surrounding tissues and close observation for a long period of time. Others advise radical excision of the glands of the related side and in the invasive cases also possible removal of the jugular vein.⁶ Lahey,¹¹ has advised that radical removal of the glands of both sides with the jugular vein is perhaps too dangerous and of too little value to be considered a standard procedure.

Hemithyroidectomy, taking the related side and the isthmus along with the nearby glands, is considered valuable treatment and perhaps especially desirable in that one need not feel too disturbed about the nerve if only one side is to be done. This is to be followed by X-ray therapy and continued observation. Crile¹ and others have adopted the procedure of feeding thyroid in moderately large dosage indefinitely to people who have had thyroid carcinoma. Metastases have been seen to become smaller under this therapy. Radioactive iodine is of value in cases with metastases only after the normal gland tissue has been completely obliterated.² This may be done either by surgery and X-ray treatment or the use

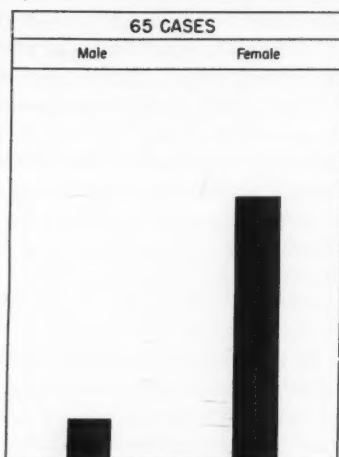


FIG. 1. Comparison of sexes

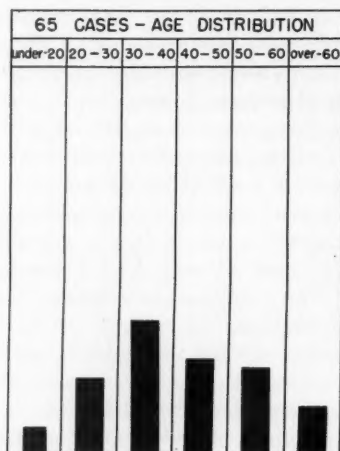


FIG. 2. Comparison of ages in decades

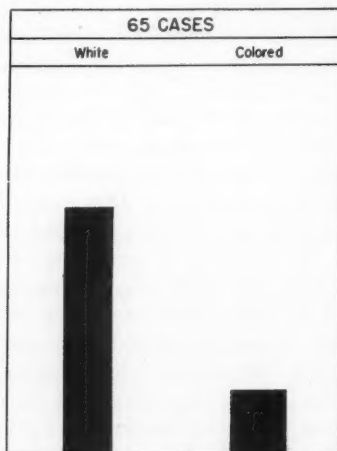


FIG. 3. Comparison of racial findings

subsequently of the thiourea drugs or a combination either of two or all three of these measures.

It is reasonable to consider one thing in reference to the surgical treatment about which little is said. The medical treatment has improved very definitely. Over a period of years it has seen an improvement of the thiourea drugs, the understanding of iodine, and its uses preoperatively, and of course the use of radioactive iodine. At the same time the understanding and improvement in the surgical procedure has been very marked. The operation done in most clinics now is anatomically reasonable and procedures are done under anesthetics that are considerably improved over the last 5 to 10 years. The fear of intense bleeding, the fear of nerve injury is less acute than previously and the occurrence is less frequent. Larger amounts of thyroid are being removed by more surgeons with less possibility of recurrence and less danger of destroying parathyroid tissue or injuring the recurrent laryngeal nerves. In the large clinics where there

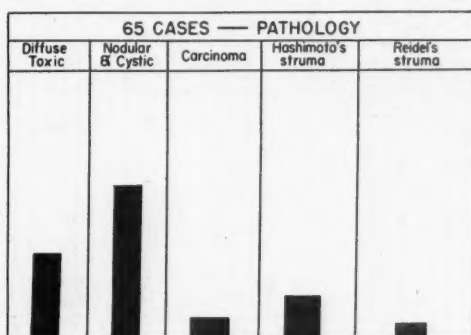


FIG. 4. Comparison of pathologic findings

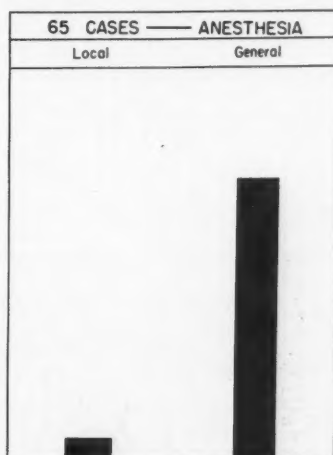


FIG. 5. Comparison of anesthesia

have been many goiters, the mortality is well below 1 per cent.^{10, 15, 18} In the small series of cases in the smaller hospitals, the results are not far from this, so, while the medical treatments have improved, the case for thyroidectomy has improved also.

From the point of view of the surgeon in the small clinic, one encouraging facet of the thyroidectomy statistical picture is the universality of results under similar treatment. The percentages of mortality; carcinoma; recurrence and apparent cure vary but little, whether obtained from a large or a small number of cases.

NORTHAMPTON-ACCOMAC MEMORIAL HOSPITAL, NASSAWADOX, VA.

ROOM No. 305

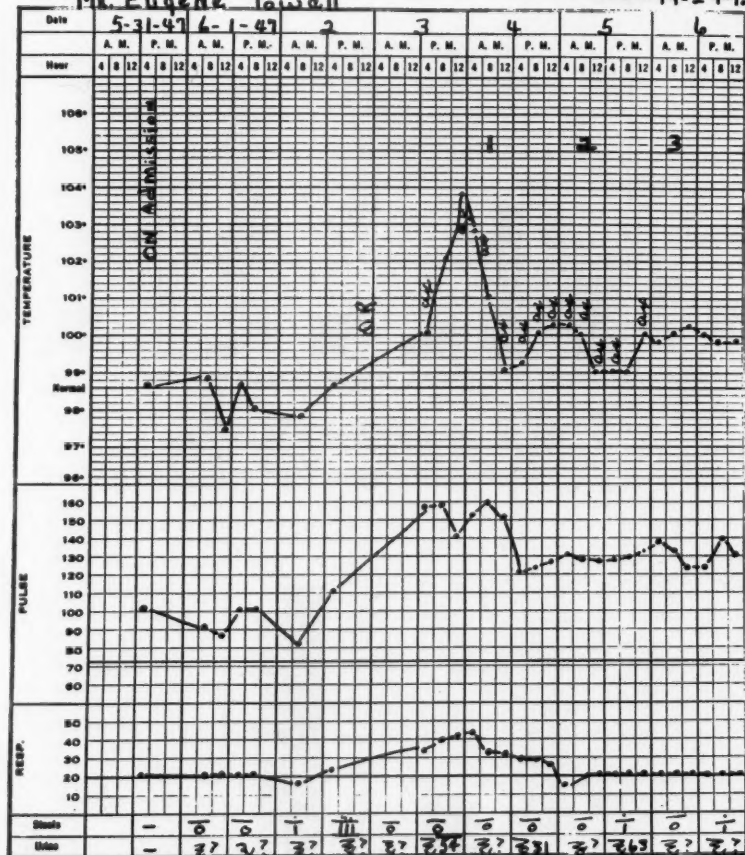
GRAPHIC CHART

SERVICE OF

DR. Denoon-Henderson

Sturk Case No. 19-24-129

NAME Mr. Eugene Powell



Form 110

Denoon, Henderson, & Co.

FIG. 6. Chart of patient, male, 17 years old in postoperative thyroid crisis with recovery

In our own small series of cases, 65 have been reviewed between the years 1932 and 1955 in nearly consecutive order.

One death occurred. This apparently was a pulmonary embolism without warning, occurring 24 hours after operation.

There were no cases of tetany or nerve injury. Two patients had a malignancy; both papillary adenocarcinoma. One died at 16 months, the other is alive after 1 year, and, we believe, free of disease. Two patients with recurrence were reoperated upon. The one who had a thyro-cardiac condition is alive and fairly well after many years; the other was the mortality noted above.

No severe or persistent myxedema has been seen. Among these patients 2 were thought to have Hashimoto's disease—1 Langhans' struma, and 1 Riedel's struma—were operated upon because of constrictive symptoms.

One patient had a thyroid crisis on the first postoperative day before the thiourea drugs or cortisone were available.

SUMMARY

The literature has been reviewed and a basis sought for decisions and indications and a brief series of cases has been partially analyzed and reported.

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SUCCESSFUL SURGICAL CORRECTION OF HERNIA OF
THE FORAMEN OF WINSLOW: WITH COMMENTS
ON THE ROENTGEN DIAGNOSIS

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Intestinal obstruction remains one of the deadly threats to life. The more frequent obstructing lesions are tumors, hernias, and adhesions. Less frequent offenders are anomalies of rotation and maldevelopment of the intestinal tract. A particularly interesting variety of obstruction is that related to internal herniation through the foramen of Winslow.

Herniation through the foramen of Winslow is rather rare. In 1924 Ullman¹³ reported that only 30 cases had been verified by operation or autopsy. Hansmann⁹ in 1939 reported on 467 intra-abdominal hernias and only 37 of these, or 8 per cent, were through the foramen of Winslow. As to diagnosis, Ullman doubted that a preoperative diagnosis ever would be made. However, Douglas⁷ a few years later, reported a successfully managed case, in which the diagnosis had been made preoperatively. Other successfully treated patients were Engstad's⁸ whose cases were reported in 1919 and Dodson's⁶ patient who was treated in 1930. While occasional successes have occurred, Watson¹⁵ regarded operation for herniation through the foramen of Winslow as having the highest mortality rate of all internal hernias.

According to Moynihan¹⁰ the foramen probably is potential rather than actual. Its anterior and posterior ligaments are as a rule in contact with one another. It seems almost certain that in order to permit the occurrence of this form of hernia there must be some gross congenital abnormality. Moynihan then lists the causes as follows: (1) a common mesentery for the whole intestine; (2) absence of the secondary fusion of the ascending colon to the posterior abdominal wall; (3) abnormal length of the mesentery, and consequently undue mobility of the intestine; and (4) abnormally large size of the foramen of Winslow.

The first record of a case in which a hernia entered through the epiploic foramen was made by Blandin³ in 1834. He observed at autopsy a large segment of the small intestine in an opening in the transverse mesocolon, its point of exit from the bursa omentalis through the epiploic foramen. Treves¹² in 1888 reported an operation at which he found the cecum, ascending colon part of the transverse colon, and between 2 and 3 feet of ileum, had passed through the epiploic foramen. He noticed that the cecum was of the undescended type, and had led the hernia into the lesser sac. A part of the hernia reappeared in the greater sac through an opening in the gastrohepatic omentum. The appendix was found at the lesser curvature of the stomach near the esophagus.

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Zimmerman¹⁷ wrote that "the original concept of the genesis of these hernias was that the incarceration occurred by the entrance of a loop of bowel into one of the numerous peritoneal fossae which perhaps was somewhat larger than usual. The concept is parallel to the usual course of events in the case of an external hernial opening. It was assumed that by a process of gradual stretching of the pocket, more and more of the bowel entered until a greater length, if not the entire small intestine, was so swallowed. Andrews¹ however, suggested that this concept was erroneous and that most, if not all, fossal internal hernias are actually anomalies of rotation and development. Andrews reasoned that at least the duodenal types of hernias and probably also the cecal, are actually anomalies of intestinal rotation in which the small bowel is trapped behind the transverse mesocolon, as the cecum rotates from the left to the right side of the abdomen and eventually becomes fixed together with the ascending colon to the posterior peritoneum".

Wangenstein¹⁴ pointed out that the entire mobile small intestine and a large portion of the colon may find its way through the foramen of Winslow into the lesser peritoneal sac. "The condition may appear at any age, the youngest having been 5 years and the eldest aged 77. The symptoms of obstruction apparently develop moderately slowly. In several cases the pain has been moderately severe; there has been little or no vomiting. The important feature in the management of these cases is early recognition that a serious lesion exists and early resort to operation. The absence of a good deal of intestine from the free peritoneal space and the presence of a cyst-like mass in the upper right abdomen at operation should establish the diagnosis".

CASE REPORT*

B.G., a 34 year old Negro woman, was admitted to the hospital on Dec. 31, 1954 complaining of cramping epigastric pain of 2 days duration. The pain had come on suddenly following a heavy meal and had continued intermittently for 24 hours when she began to vomit. She had passed no flatus nor had a bowel movement since the onset of her pain. She was in her fifth month of pregnancy and denied abnormal symptoms or signs referable to this gestation despite the fact that approximately 3 months previously she had attempted abortion on one occasion by taking an overdose of quinine and on another by "catheter" manipulation. Physical examination revealed a soft abdomen without distention or abnormal mass. There was slight epigastric tenderness but no rebound tenderness and bowel tones were considered to be within normal limits. She was afebrile with white blood cell count of 9,500 per cu. mm. and normal differential. Her urinalysis was normal. Serum amylase was 68 units. Chest roentgenogram (fig. 1) was clear and there was no free air under the diaphragm.

She was treated as a peptic ulcer problem pending further studies. However, she continued to vomit and began to have abdominal distention of moderate degree. Surgical consultation was requested on Jan. 4, 1955, at which time the story was obtained that she had had no bowel movements, or flatus since the onset of her epigastric pain 6 days previously and that intermittent colicky pain had continued. She had remained afebrile. On January 4 a roentgenogram (fig. 2) of the abdomen showed small bowel obstruction, gastric distention and an epigastric air shadow thought to be air containing viscus. The patient was treated

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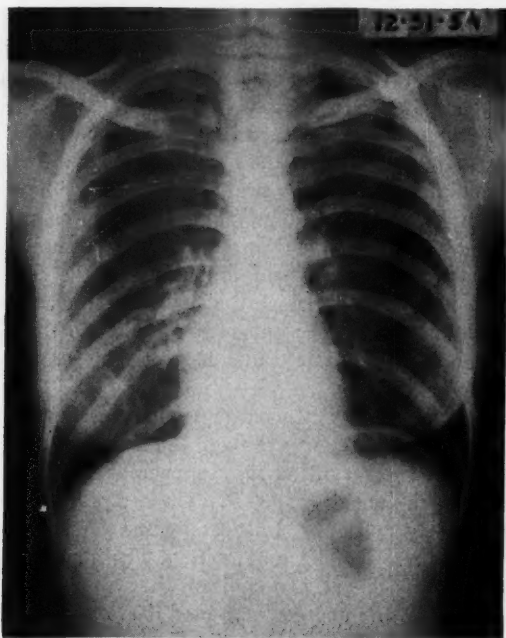


FIG. 1. Admission chest film showing crescentic subdiaphragmatic air shadow with rugal folds considered normal. Second gas shadow lower down suggests a segment of colon and is not unusual in appearance.

with Cantor tube suction and intravenous fluids but the tube could not be advanced beyond the pylorus. On January 6, her white blood cell count was 11,500 per cu. mm. and a repeat roentgenogram (fig. 3) of the abdomen showed decompression of the stomach without improvement in the small bowel distention. However, the epigastric radiolucency persisted. The radiologist thought this might represent herniation of the small bowel through the foramen of Winslow. The fetal skeleton was considered deformed and it was believed that the fetus was dead.

Exploratory laparotomy (by D.H.D.) through a midline epigastric incision was done on January 7 revealing distention of the entire small bowel. This was decompressed by aspiration. Exploration of the epigastrium disclosed a small abscess between the gastrohepatic ligament and the anterior abdominal wall slightly to the left of the midline. The gastrohepatic ligament "bulged" anteriorly, was indurated and erythematous with pus coming through a small 3-4 mm. opening near the incisura of the stomach. The ligament was incised releasing a large amount of mixed pus and fecal material. This was contained in an abscess cavity which communicated with a perforation in the anterior wall of the cecum approximately 7-8 cm. distal to the ileocecal valve. The cecum and distal terminal ileum had herniated through the foramen of Winslow and had become incarcerated in the lesser sac with subsequent perforation (fig. 4). The contents of the cecum were evacuated through a 5 cm. transverse incision which then was closed with a running catgut suture. The incarcerated bowel then was manually reduced through the foramen of Winslow back into its normal position in the abdominal cavity. This herniation was possible because there was congenital malrotation of the colon. The entire right colon and terminal ileum were not anchored to the posterior abdominal wall in the usual manner and were unrestricted in



FIG. 2. Scout film of abdomen 4 days after admission showing gaseous distention of small bowel and large collection of gas in the epigastrium. In retrospect, the faint air-outlined lumen of the displaced stomach can be identified (arrows). Note bizarre appearance of fetal skeleton in pelvis.

their movements about the abdominal cavity. The uterus was compatible with a normal 5 months gestation. No fetal movements could be felt.

The appendix was grossly inflamed. Appendectomy was performed. The incarcerated portion of the cecum was edematous and hemorrhagic, but viable. The incision which had been made in the cecum at the site of the perforation was reinforced with a transverse row of interrupted Lembert no. 0000 silk sutures.

The abdominal cavity was thoroughly irrigated with warm normal saline solution and a Penrose drain was brought out through the right upper quadrant from the foramen of Winslow. A Chaffin tube was placed in the lesser sac through a stab wound in the gastrocolic ligament and brought out through the abdominal wall in the left upper quadrant. The abdominal wound was closed with no. 20 stainless steel wire.

Terramycin was dripped intermittently into the peritoneal cavity through the Chaffin tube for 4 days. Achromycin was given intravenously. The patient had intermittent low grade fever (Temp to 101°F maximum) for 10 days and then remained afebrile thereafter. The white blood cell count rose to a high of 28,300 per cu. mm. on January 12 at which time fluid in the left costophrenic angle and elevation of the diaphragm was demonstrated. She was taking a soft diet and was having normal bowel movements. She was fully ambulatory. Fetal movements were noted on the fifth postoperative day. The patient's serum chemistry was maintained at normal levels throughout her convalescence. She was con-



FIG. 3. Follow-up film of abdomen after passage of radiopaque tube which established the lateral displacement and compression of the stomach by huge gas collection corresponding to the lesser sac. Note increasing distention of small bowel and continued bizarre appearance of fetal skeleton.

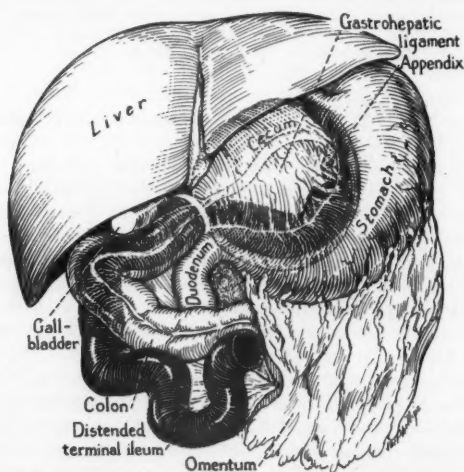


FIG. 4. Semidiagrammatic reproduction of the operative findings. The cecum, approximately one-half of the ascending colon and the terminal ileum had herniated through the foramen of Winslow and were incarcerated in the lesser sac. The cecum and proximal small bowel were markedly distended. The normal peritoneal attachments of the ascending colon and terminal ileum were absent as is commonly seen in malrotation of the colon. Perforation of the cecum had occurred producing an abscess in the lesser sac.

tinued on oral antibiotics and the pleural fluid gradually disappeared. The diaphragm returned to its normal position. She was discharged on January 25, 25 days after her admission to the hospital, afebrile without complaint with a normal pregnancy and she was gaining weight. She has subsequently delivered a normal healthy baby.

ROENTGEN DIAGNOSIS

Preoperative diagnosis of this rare condition is mainly dependent upon roentgen examination and should be relatively easy. The lesser sac occupies a fixed position within the abdomen and normally is only a potential space. When it contains gas only three types of abnormality are possible; pneumoperitoneum, abscess with gas formation, and herniation of gas containing bowel into the sac, via the epiploic foramen or a tear in one of the walls making up the lesser sac.

Recognition of gas in the lesser omental sac is not difficult if the stomach and normally placed transverse colon can be distinguished from a spherical accumulation of gas in the epigastrium, centered slightly to the left of the midline. Lateral filming, contrast material, or, as in this case, a radiopaque suction tube may be necessary to identify and locate stomach and colon positively. Apparently, the single supine film of the abdomen is highly suggestive although the rare occurrence of this condition and even more infrequent preoperative roentgen demonstration provide few illustrations in the literature.

Having determined the presence of gas in the lesser sac, differentiation of the cause is somewhat more difficult. Simple pneumoperitoneum is most frequent from recent laparotomy or ruptured hollow abdominal viscus. Abscess in the lesser sac as a result of a ruptured viscus probably could not be differentiated from pneumoperitoneum except by the history and clinical findings. In both cases gas in the general peritoneal cavity is likely. In neither case is typical mechanical obstruction likely and this finding then becomes a differential point in herniation of bowel into the lesser sac. The chief diagnostic points for such an interpretation are: (1) rounded accumulation of gas in the epigastrium separate from the stomach; (2) displacement of the stomach to the left; (3) deformity and compression of stomach corresponding to a mass in the lesser sac; and (4) signs of mechanical bowel obstruction.

Helpful findings include: (1) demonstration of mucosal pattern lining gas in the lesser sac; (2) absence of cecum and colon from right abdomen, when these are involved in hernia; (3) tapered or pointed efferent limb of colon through the foramen as demonstrated by barium enema; and (4) demonstration of rather typical gastric mucosa when stomach contains air as helpful evidence that the more centrally located gas is not within the stomach.

When adequate roentgen examination of the abdomen is feasible preoperatively the correct interpretation should be possible. In this instance all of the criteria were met except that mucosal markings were not demonstrable in the herniated portion of the intestine; perhaps this is attributable to perforation and abscess formation. The correct interpretation was suggested although lack of prior experience and the infrequency of the condition prevented a dogmatic diagnosis. Further roentgen examination was not deemed advisable prior to surgery.

An interesting side light is the misinterpretation of fetal death, which, in retrospect, can be attributed to the marked displacement of fetal skeleton by gas filled loops of bowel producing an "end on" view simulating the grotesque and compressed appearance commonly found in fetal death. The lack of over-riding or overlapping of cranial sutures should have prevented such an impression, as the record states a normal healthy infant was subsequently delivered.

DISCUSSION

The diagnosis of herniation through the foramen of Winslow is important in order to establish treatment early. The herniation causes a mechanical obstruction which is not amenable to intestinal intubation, the obstruction is a closed loop form with regard to the contents of the lesser sac. The disturbance around the pylorus and duodenum with compression of this area results in lessened passage of swallowed air into the small intestine, and also hinders the vomiting of small bowel contents. Again, the effect is somewhat like a closed loop between the contents of the lesser sac and the pylorus. Hence, there is in effect the possibility of two closed loops being present in these cases. The lack of fecal vomiting and the late development of bowel distention may be attributed to these factors, moreover, it is apparent that intubation of the small bowel past the pylorus will be difficult (it was not possible in this case) and consequently will be unsuccessful in relieving the small bowel obstruction. The high incidence of incarceration, gangrene, and death in this form of closed loop obstruction is dependent upon the peculiar anatomic characteristics of this type of hernia, which are responsible for the slow onset of symptoms and delay in recognition and treatment.

SUMMARY

An instance of the successful management of a strangulated hernia of the foramen of Winslow is reported. Despite the rarity of the condition, awareness of certain roentgen findings may suggest the correct diagnosis preoperatively. These are: (1) rounded accumulation of gas in the epigastrium separate from the stomach; (2) displacement of the stomach to the left; (3) deformity and compression of the stomach corresponding to the mass in the lesser sac; and (4) signs of mechanical bowel obstruction.

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A SURVEY OF EXPERIENCES WITH THREE HUNDRED CLINICAL AND ONE HUNDRED AND EIGHT AUTOPSY CASES OF ACUTE PANCREATITIS*

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At the present time we are engaged in the process of reviewing all clinical and autopsy material on acute inflammatory diseases of the pancreas collected during a period of over 25 years. Thus far we have concluded an analysis of 300 such cases, the clinical aspects of which are herein reported along with data tabulated from autopsy material. The latter consists of a series of 2,559 consecutive necropsies, including 108 additional cases of acute pancreatitis. Findings are presented for the purpose of relating observations to etiology, diagnosis, therapy and complications.

CLINICAL TYPES

These cases fall conveniently into four categories, which are defined as follows:

1. *Transient Pancreatitis*. These are typical cases of acute pancreatitis with diagnosis supported by a transient elevation of serum diastase values. These patients go on to complete recovery without complications, as described by Gray, Probststein and Heifetz.⁵

2. *Secondary Pancreatitis*. These are cases in which the acute inflammatory disease of the pancreas is due to extension of an inflammatory process from another site. In general, these are secondary to posterior duodenal ulcers, perforated gastric or duodenal ulcers with peritonitis, extension of peritonitis from a perforated viscus not in the vicinity of the pancreas, and acute postoperative pancreatitis as recently described by Dunphy and associates,³ and others.

3. *Fulminating Pancreatitis*. These are cases of pancreatitis in which the patients exhibit marked shock and which terminate fatally. This category is more commonly known as "acute hemorrhagic pancreatitis" and pancreatic apoplexy.

4. *Terminal Pancreatitis*. This is a group recently defined by Sachar and Probststein.¹⁰ It is characterized by a mild form of acute interstitial pancreatic inflammation along with small foci of fat necrosis incidentally discovered at autopsy. For the most part, such patients die of cardio- or cerebrovascular disease.

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Presented during the Kansas City assembly of The Southwestern Surgical Congress, Kansas City, Mo., September 5-7, 1955.

These investigations were aided by grants from the David May-Florence G. May and the Louis Monheimer Memorial Research Funds.

ETIOLOGY

Although many theories have been presented in the last half decade dealing with causal factors in acute pancreatitis, they may be consolidated into four major categories as follows:

1. The Common Channel Theory.
2. The Inflammatory Theory, including the reflux of gastric or duodenal contents.
3. The Toxic or Metabolic and Traumatic Theories.
4. The Vascular Theory.

It is not our intention here to review experimental and clinical evidence supporting each of these concepts, but rather to show what clinical information of etiologic significance may be derived from our cases.

1. *Common Channel Theory:* As shown in table I, in 8.5 per cent of all our clinical cases, acute pancreatitis was found in association with a common duct stone. Similarly, in the 108 autopsied cases of acute pancreatitis, 9 (8.3 per cent) showed common duct obstruction, 4 by a calculus and 5 either by an intrinsic tumor of the biliary tract or from compression by an extrinsic tumor, as compared with 3.3 per cent in the total autopsy population. These findings agree favorably with the observations of Dragstedt and co-workers,² who estimated that about 10 per cent of cases can be accounted for on this basis.

However, these investigators have also estimated that an additional 50 per cent may possibly be accounted for on the basis of inflammatory disease of the biliary tract, involving the sphincter of Oddi, thereby producing an obstruction or stenosis, which would in effect produce a common channel. It is generally assumed that chronic gallbladder disease with cholelithiasis may lead to such a development. However, only 26.8 per cent of the patients of our clinical cases showed evidence of chronic cholecystitis with cholelithiasis. On the other hand, 6 per cent of our patients had cholecystectomies from 10-20 years before their initial attack of acute pancreatitis, and in these there was no evidence of recurrent inflammatory disease of the biliary tract. On a necropsy basis, 12 per cent of the total autopsy population showed chronic cholecystitis with cholelithiasis, as compared with 15.7 per cent in patients with acute pancreatitis. This is not a significant difference. Similarly, 2.4 per cent of the total autopsy population had had a cholecystectomy prior to death, as compared with 2.8 per cent in necropsied cases with acute pancreatitis. As regards acute cholecystitis, in autopsied cases this disease was found in 1.3 per cent of the total group as compared with 3.7 per

TABLE I

Frequency and types of biliary tract disease associated with acute pancreatitis

Disease	Clinical Pancreatitis	Autopsy Pancreatitis	Total Au- topsy Group
Common duct obstruction	8.5	8.3	(3.3)
Chronic cholecystitis with cholelithiasis	26.8	15.7	(12.0)

cent of the cases of acute pancreatitis. This last comparison contains too few cases of acute pancreatitis to permit proper evaluation at present.

These autopsy data, in particular, do not support the generally accepted idea that the incidence of chronic cholecystitis with cholelithiasis is significantly higher in acute pancreatitis than in the general population. On the other hand, it is evident that about 9 to 10 per cent of cases of acute pancreatitis fit into the common channel theory as originally proposed by Opie.

2. *The Inflammatory Theory:* In general, this theory attempts to account for those instances in which no obstruction of the sphincter of Oddi cannot be demonstrated. It has been postulated that the reflux of duodenal content into the pancreatic ducts may introduce infectious material into the pancreas and thus precipitate acute pancreatitis. While there is no clinical evidence to support such a contention, disturbances of motility of the duodenum incident to the presence of an ulcer might conceivably account for such an event. On a clinical basis, 3.6 per cent of our patients might fit into the latter category, since they showed a duodenal ulcer in association with acute pancreatitis.

This concept of the etiology of acute pancreatitis also includes instances of hematogenous infections and septic embolization, which may incidentally involve the pancreas, as well as certain viral infections. Three of our autopsied cases (2.8 per cent), as shown in table II, fit into the former category. As to a viremia with pancreatic involvement, we have only one case of mumps in the present group of cases. In one series, Brahdy and Scheffer¹ have reported 2.4 per cent as a complication of this disease, and in another Egdahl⁴ has observed 10.5 per cent. In addition, 3.7 per cent of autopsied cases of pancreatitis were associated with viral hepatitis, as compared with an incidence of this hepatic disease in the general autopsy population of 0.9 per cent.

By far the most common type of infectious pancreatitis in our autopsy series (11.1 per cent) was that associated with intra- or retroperitoneal suppuration. As shown in table II, this was most often a complication of perforation of a gastric or duodenal ulcer, or of a viscus distant to the pancreas. The latter was the result of a perforated appendix or of a diverticulitis of the colon with generalized peritonitis. Disruption of the duodenal stump with peritonitis following gastrectomy was noted in 2.8 per cent of our autopsied cases with acute pancreatitis. In one autopsy case a perinephric abscess extended into the pancreas and produced acute pancreatitis.

TABLE II
Frequency of acute infectious pancreatitis

Source of Infection	Per Cent in Autopsied Series of Acute Pancreatitis
Bacteremia or septic embolization	2.8
Viral hepatitis	3.7 (0.9)*
Perforated gastric or duodenal ulcer	3.7
Perforated viscus distant to pancreas	3.7
Perinephric abscess with extension to pancreas	0.9

* Per cent in general autopsy population.

Also pertinent to the infectious theory of pancreatitis are 2 cases observed by Longmire, in which distantly located aberrant pancreas also showed acute necrosis, since such an event could conceivably occur on the basis of a bacteremia or septic embolization, although there was apparently no clear-cut evidence for either event. The possibility of a circulating toxic factor to which pancreatic tissue would be peculiarly susceptible cannot be excluded.

In general, our observations appear to indicate that the capsule of the pancreas can be penetrated by an acute infectious process, even in the absence of trauma, with a resulting acute pancreatitis. Eight and three-tenths per cent of our autopsied cases fall into this category. In those cases of infectious pancreatitis following gastrectomy and disruption of the duodenal stump, the factor of trauma in injuring the capsule cannot be excluded (2.8 per cent). Another 3-7 per cent of our autopsied cases of acute pancreatitis appear to be on the basis of viremia. In total, 14.8 per cent of our cases of acute pancreatitis coming to autopsy appear to be on an infectious basis.

3. *Toxic or Metabolic and Traumatic Theories:* There were no instances either in the series of clinical cases of pancreatitis or those coming to autopsy in which toxic factors could be clearly implicated.

In this regard, as shown in table III, cirrhosis of the liver of significant degree was present in 7.4 per cent of our cases of acute pancreatitis coming to autopsy, as compared with 4.6 per cent in the general autopsy population. Impairment of the detoxication function of the liver might also be assumed in malignant disease involving this organ, but the frequency of primary or secondary tumors of the liver was greater in the general autopsy population than in the cases of acute pancreatitis. In general, icterus on a hepatic basis was about three times more frequent in association with acute pancreatitis than in the general autopsy group. However, of the approximately 20 per cent of autopsy cases with pancreatitis associated with icterus, about 8 per cent can be accounted for on the basis of obstruction of the common bile duct, about 7 per cent on the basis of cirrhosis, and an additional 3 per cent on the basis of viral hepatitis. This leaves less than 2 per cent to be accounted for by other diseases.

As to trauma, there was only one case which was autopsied in which acute pancreatitis followed an episode of trauma. There were 3 additional cases of post-gastrectomy pancreatitis without significant peritonitis similar to that recently reported by Millbourn,⁷ by Warren,¹¹ and by Dunphy and associates.³ Trauma might therefore account for about 3.7 per cent of our cases of acute pancreatitis coming to autopsy.

TABLE III
Association of hepatic disease with acute pancreatitis

Hepatic Disease	Per Cent in Autopsy Group	
	General Autopsy Population	Acute Pancreatitis
Cirrhosis	4.6	7.4
Malignancy	11.3	9.2
Hepatogenous Icterus	5.4	20.4

TABLE IV
Age Distribution in Acute Pancreatitis

Age Group	Per Cent	
	Clinical Cases	Autopsy Cases
0-10 years	0	3.5
11-20 years	0	0
21-30 years	8.6	1.7
31-40 years	11.0	6.1
41-50 years	17.1	21.1
51-60 years	30.0	17.5
61-70 years	17.1	30.7
71-80 years	13.4	15.8
Over 80 years	2.4	3.5

4. *Vascular Theory:* According to Ivy and Gibbs⁶, there is no evidence to indicate that impairment of blood supply occurs with significant frequency as an initiating factor in human pancreatitis, although there is some evidence that transient interference with the arterial blood supply to the pancreas may be a contributing factor. The vascular lesions described by Rich and Duff⁹ should be considered as the result of the action of pancreatic enzymes on vessel walls following the initiation of the inflammatory process. Without attempting to resolve these conflicting views, we should like to present one striking tabulation.

Within the limits of expected variability, this table shows essentially the same age distribution in both the clinical and the autopsied series which we have observed in cardio- and cerebrovascular disease, with the greatest frequency between the ages of 41 and 70.

This observation strongly suggests some role for a vascular factor, although its relative importance remains to be determined. As a result of this investigation we are now engaged in a study of aging changes in pancreatic arteries and their possible relation in the pathogenesis of pancreatic disease. Lending promise to such an investigation is the fact that certain lesions included in the category of "acute hemorrhagic pancreatitis" have long been recognized as resembling infarcts in their distribution as well as gross and microscopic features. It should also be pointed out that although terminal pancreatitis represents a relatively mild form of the disease, it is most frequently associated with cardio- or cerebrovascular deaths.

Symptomatology in Clinical Cases

Abdominal pain was present in almost all cases, but in a few (0.9 per cent) there were no symptoms referable to the abdomen. Most of these were in cases of terminal pancreatitis, and in a few instances of fulminating pancreatitis. Abdominal rigidity, on the other hand, is a relatively infrequent symptom, occurring in only about 1 case in 6. Fever ranging from 100 to 104 occurred in about half of our patients, and vomiting in about one-third. Jaundice was present in about one-fifth of the patients, thus corresponding to the autopsy data, although common duct obstruction was present in only slightly over 8 per cent.

TABLE V
Frequency of common signs and symptoms

Abdominal pain	95.1 per cent
Abdominal rigidity	15.9 per cent
Fever	51.2 per cent
Vomiting	33.0 per cent
Jaundice	19.5 per cent

TABLE VI
Analysis of abdominal pain

Localization	Per Cent
Epigastric	11.0
Right upper quadrant	23.4
Generalized	50.0
Lower abdomen	6.1
Left upper quadrant	4.9
Radiation	Per Cent
To back	35.9
To shoulders	3.6
To left chest	2.4
To right side	10.5
To both sides	1.2

Most investigators describe the pain of acute pancreatitis as being in the upper abdomen. This was true in about three-fourths of our patients. Surprisingly, slightly over 6 per cent have pain in the lower abdomen. Radiation is generally described as either penetrating to the back or to the right or left shoulder. Radiation was experienced in about one-half of the patients, with the back the most frequent site. Radiation to the shoulders was experienced by relatively few patients. In our experience pain appeared to come on at times insidiously, with an increase in tempo of severity, and to persist for hours or for days; sometimes it made its appearance so suddenly and acutely as to put the patient in shock. Pancreatitis should be suspected whenever the patient complains of any type of abdominal pain, but particularly if the pain is in the upper abdomen. There is, thus, no constant typical picture of pancreatic pain.

The most simple, useful and reliable tool for the diagnosis of acute pancreatitis remains the serum diastase determination. A useful accessory tool is the urine diastase output per hour, which gives certain useful information. We should, however, like to discuss the data shown in table VII from a prognostic as well as diagnostic point of view. It is apparent that, on the average, the fulminating type of pancreatitis gives the highest serum diastase values, while generally, no distinction appears possible on the basis of this determination between transient and secondary pancreatitis. The range of variation indicates, however, that in individual cases it may not be possible to attach prognostic value to this laboratory

TABLE VII
Average serum diastase levels in various types of acute pancreatitis

Disease Type	Frequency	Average Diastase Level
Transient	72.2 per cent	1410 (148-5500)
Secondary	11.8 per cent	1193 (474-2940)
Fulminating	9.0 per cent	2982 (1300-7594)
Terminal	7.0 per cent	282 (125-675)

result, since there is considerable overlap between the first three types of pancreatitis shown in the table. As we shall point out, these observations also have therapeutic implications.

Therapy

In a number of our publications we have pointed out that conservative, supportive therapy without operative intervention, is the treatment of choice in acute pancreatitis. On a statistical basis, since about three-fourths of our patients are of the transient type, such a conclusion seems logical. However, on an individual case basis the diastase level affords no certainty for differentiating between the three most frequent clinical types. This becomes particularly important in certain instances of secondary type, such as a perforated viscus, when operative intervention may be indicated. Operative intervention is also obviously indicated in those instances in which acute pancreatitis may be on a common channel basis with an obstruction due to a calculus.

Complications

While recurrence of attacks may not be considered a complication in a limited sense, it has special significance with regard to the etiology of chronic recurrent pancreatitis with calculi. Seven and four-tenths per cent of our patients had attacks of acute pancreatitis, and 15.8 per cent had 3 or more attacks of this disease. Together, then, almost one-fourth of our patients had more than one attack. Yet we have not encountered a single instance of chronic pancreatitis with calculus formation and pancreatic insufficiency in the more than 25 years which this series covers. We should like to present herewith, by way of illustration, an instance of a patient who had seven proved attacks of acute pancreatitis and eventually came to autopsy.

This patient, a white man, was first seen in 1927, at the age of 34, with symptoms of chronic cholecystitis with gallstones, and about 7 months later a cholecystectomy was performed. He was readmitted in 1932, 1933, 1937, 1942, 1945 and 1946, and each time a diagnosis of transient acute pancreatitis was made and proved by elevated serum diastase levels plus other clinical data. He was readmitted for the last time in May of 1954, and died of a cerebrovascular accident. At autopsy sections of pancreas showed marked fibrosis, apparently the result of scarring following recovery from previous acute attacks, and infiltration of acute and chronic inflammatory cells in adjacent peripancreatic fat and interstitial

connective tissue. Ducts showed no remarkable dilatation and there was no evidence of calculi.

From these and previous observations we are unable to establish any relationship between so-called chronic relapsing pancreatitis with stone formation and repeated attacks of acute pancreatitis. The former appears to be a separate entity, with etiology and pathogenesis unrelated to acute pancreatitis.

Pancreatic abscess has been a relatively rare complication, having occurred only four times in the combined clinical and autopsy series (408 cases). We have recently reported 12 instances of pseudocyst, which represents the total observed in this series, and have treated some of these successfully by the Juraes procedure of internal drainage. However, the question whether or not these represent a complication of acute pancreatitis remains unresolved despite the fact that several of these patients gave a history strongly suggestive of previous bouts of acute pancreatitis.

SUMMARY AND CONCLUSIONS

Our experiences with acute pancreatitis covering a period of over 25 years have been presented. This includes 300 clinical cases and 108 additional cases which came to autopsy. Etiologic inferences which may be drawn from clinical observations have been dealt with and we have also reviewed various aspects of clinical signs, diagnostic methods, therapy, complications and prognosis.

It is apparent from the data in this report that no single etiologic factor can explain all cases of acute pancreatitis. About 8 to 10 per cent appear to develop on a "common channel" basis, another 10 per cent on an infectious basis, and approximately 10 per cent on a toxic, metabolic or traumatic basis. Chronic gallbladder disease with lithiasis does not appear to have an increased frequency in acute pancreatitis. This leaves unexplained the etiology in almost two-thirds of the cases.

These statistical data further indicate, from a therapeutic standpoint, that the treatment of choice, particularly in transient and fulminating pancreatitis, remains a conservative one. The common channel type should be treated surgically, as should those types of infectious pancreatitis secondary to a perforated viscus.

Our observations also indicate that chronic relapsing pancreatitis is not a complication of recurrent acute pancreatitis.

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CLINICAL AND EXPERIMENTAL STUDIES TO DETERMINE THE ROLE OF THE PANCREAS IN SERUM AMYLASE FORMATION*

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INTRODUCTION

Since the general usage of blood and urine amylase tests, there has been much interest in, and controversy as to their diagnostic value. There is continuing difficulty in making a correct diagnosis in acute primary pancreatitis, and pancreatitis secondary to upper abdominal surgery even when these tests are used.

In recent years, several reports^{1, 6, 8, 10, 14, 15} have appeared in the literature on postoperative pancreatitis following biliary and gastric surgery, using the amylase determination as the major criterion for the diagnosis.

For some time prior to these reports, we had been of the opinion that there must be some mechanism in addition to pancreatic injury or obstruction of the ducts that causes an elevation in the blood amylase level. The work of Gray and associates⁴ gave support to this opinion. They gave ACTH to normal individuals and found an increased excretion of uropepsinogen. In animals following total gastrectomy no such increase was obtained. They then gave ACTH to patients and found a markedly increased excretion of uropepsinogen in duodenal ulcer patients, a decreased excretion in gastric ulcer patients, and no increase in patients with pernicious anemia or diffuse gastric mucosal atrophy.

Accordingly the following working hypotheses were evolved and tested clinically and experimentally.

Hypotheses

The elevation in the serum amylase level is the result of any insult from which the anterior pituitary undergoes hypertrophy and is not specifically the result of pancreatitis or pancreatic injury except in so far as they are serious nonspecific insults.

The serum amylase level is elevated after stress by the anterior pituitary-adrenal cortical axis.

Methods

The Meyers-Free-Rosinski sugar reduction method⁹ for determining serum amylase levels was used throughout this study. The normal range by this method is 0.5-2.5 mg. per cc. of serum. Perhaps more people are familiar with the Somogyi

* Presented during the Richmond Assembly of The Southeastern Surgical Congress, March 12-15, 1956. Richmond, Va.

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This work was supported by a grant from the Samuel H. Kress Foundation to the John F. Erdmann Surgical Research Laboratory.

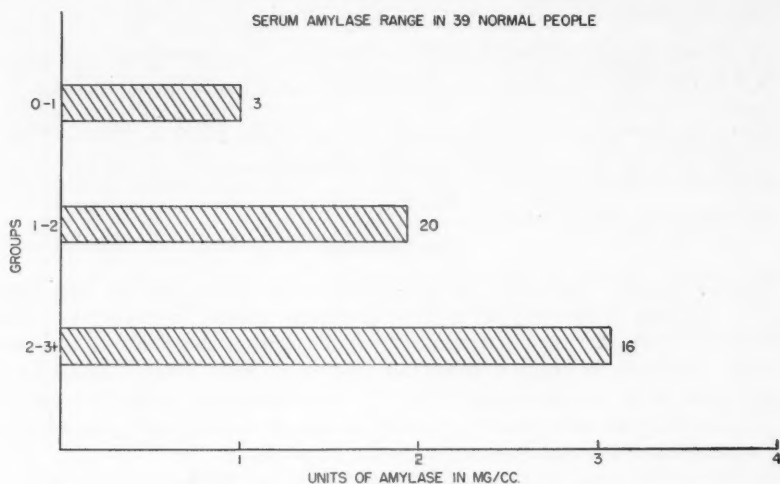


FIG. 1

technic¹³ wherein the normal range is 60–250 Somogyi units. With the Meyers-Free-Rosinski method 1 mg. approximates 100 Somogyi units.

Elman, Somogyi, and others^{2, 3, 5, 7, 9, 12} have shown that there is a narrow range in normal individuals and, indeed, this was found to be true. In 39 individuals who were not operated upon and with no evidence of pancreatic disease the range was between 0.38 and 3.07 mg. per cc. (fig. 1). This gave some assurance that the technical errors would be minimal.

Clinically, preoperative base levels of serum amylase were obtained on 100 patients. Postoperatively 3 to 20 determinations were made on each patient, including 1 on the first postoperative day. In all, 827 determinations were made. In 20 cases of acute trauma, a determination was made within 24 hours of the injury with 1 to 14 determinations being carried out. In all, 73 determinations were done. In addition, 6 human beings had normal serum amylase values established, following which each received a daily intramuscular injection of 100 units of ACTH for 7 days. The dosage was reduced to 80 units for 2 days, and then 40, 25, and 12½ units respectively for similar periods of time, giving a total of 15 days of ACTH administration. The levels of serum amylase were followed during this period.

Experimentally, 20 normal mongrel dogs were used to determine their normal range. The levels ranged from 13.5 to 78.8 mg. per cc. of serum. Daily determinations of 4 normal dogs for 3 consecutive days showed a range 45–55 mg. per cent, the greatest variation being 5.0 mg. and the least 2.5 mg. per individual dog.

Thirteen dogs were then used for ACTH injections with 2 other dogs as controls. Each dog was given a single intramuscular injection of 175 units of ACTH and daily determinations of serum amylase were carried out for an average of 12 days. A total of 229 amylase determinations were done on the 15 dogs.

Nineteen dogs were pancreatectomized, and of the pancreatectomized dogs, 3 were given a single injection of 175 units of ACTH intramuscularly with 1 as a control.

RESULTS

The 100 postoperative patients were made up of 71 cases of intra-abdominal surgery and 29 cases of extra-abdominal operations (fig. 2). The intra-abdominal cases fitted roughly into 4 groups.

The first group consisted of 9 patients who showed a rise varying between 8.0 and 17.3 mg. per cc. of serum. These included 4 cases of biliary tract surgery: 2 cholecystectomies and 2 cholecystectomies plus choledochotomy; 3 cases of subtotal gastrectomy, 1 with added cholecystectomy; 2 cases of small bowel obstruction, 1 requiring resection, the other lysis of adhesions.

The second group consisted of 18 patients who showed a rise varying between 4.0 and 8.0 mg. per cc. These included 10 cases of biliary tract surgery: 9 with cholecystectomy and 1 cholecystectomy with choledochotomy; 2 cases of subtotal gastrectomy for duodenal ulcer; 2 cases of carcinoma of the stomach, 1 a total gastrectomy, the other subtotal gastrectomy; 3 cases of carcinoma of the colon with resection; and 1 case of strangulated loop of ileum in an umbilical hernia requiring resection.

The third group consisted of 24 patients with elevation from the upper limit of normal to 4.0 mg. per cc. There were 11 cases of biliary tract surgery including 4 cholecystectomies, 6 cholecystectomies with choledochotomy, and 1 cholecystectomy, choledochotomy and subtotal gastrectomy. There were 5 gastric cases: 2

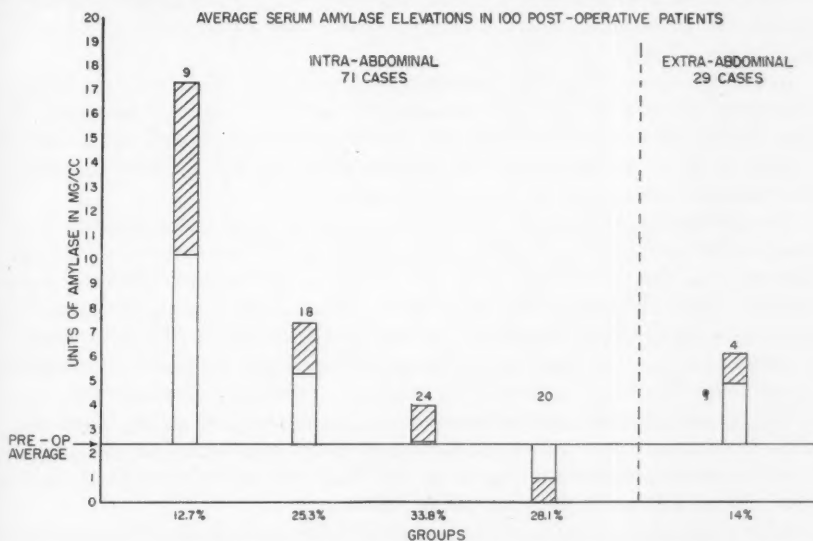


FIG. 2

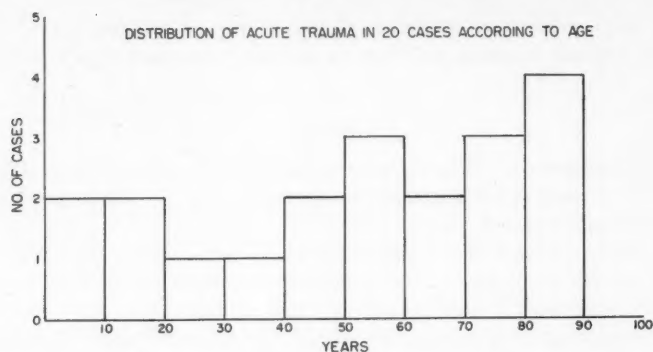


FIG. 3

closures of perforated ulcers, and 3 subtotal gastrectomies. The other cases included: 2 colon cases requiring resection; 2 of regional ileitis: 1 with resection, the other without; 1 case of abdominal carcinomatosis; 2 cases of small bowel obstruction with lysis of adhesions; and 1 sarcoma of the spleen with splenectomy, partial pancreatectomy, and resection of the splenic flexure of the colon.

The fourth group consisted of 20 patients showing an actual decrease from the preoperative range. These included 11 biliary tract cases: 9 cholecystectomies, and 2 cholecystectomies with choledochotomy. There were 6 gastric cases: 2 closures of perforated ulcers and 4 subtotal gastrectomies. The other cases were: 1 carcinoma of the pancreas, 1 cholecystojejunostomy, and 1 simple epigastric hernia. The preoperative amylase determinations varied from 4.58 to 0.61 with an average of 1.06.

In 4 of the 29 patients with extra-abdominal operations, there were elevations from 4.04 to 6.1 mg. per cc. These included 2 hemorrhoidectomies, 1 carcinoma of the thyroid, and 1 carcinoma of the mouth with radical neck dissection. The other operations were thyroidectomies, herniorrhaphies, hemorrhoidectomies, thoracotomies, and excision of tumors of the breast.

The 20 cases of acute trauma varied from 4 to 89 years in age (fig. 3). Five cases, occurring in the fourth, fifth, sixth, and seventh decades showed elevations varying from 3.45 to 7.10 mg. per cc. (fig. 4). The cases included 1 cerebral concussion, 1 fracture of hip, 1 fracture of femur, 1 fracture of tibia and fibula, and 1 multiple injuries with compound, comminuted fracture of tibia and fibula, avulsion of skin of calves and loin, and penetrating wound of loin with transection of the colon. The last case showed an immediate rise of the serum amylase.

The normal dogs given ACTH showed an average elevation of the blood amylase of 16.2 mg. per cc. of serum. The range varied from 5.5 to 23.7 mg. per cc.

Of the pancreatectomized dogs given ACTH, 3 showed increases from 4.1 to 19.2 with an average of 10.3 mg. per cc. (fig. 5).

After 6 persons were given a course of ACTH therapy, one showed a moderate rise and 4 marked elevations of the serum amylase. These results are all the more

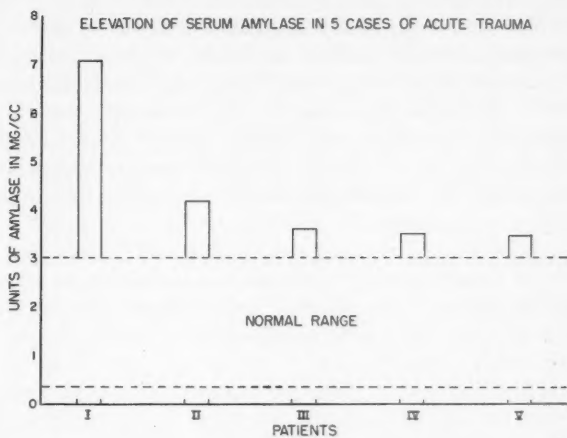


FIG. 4

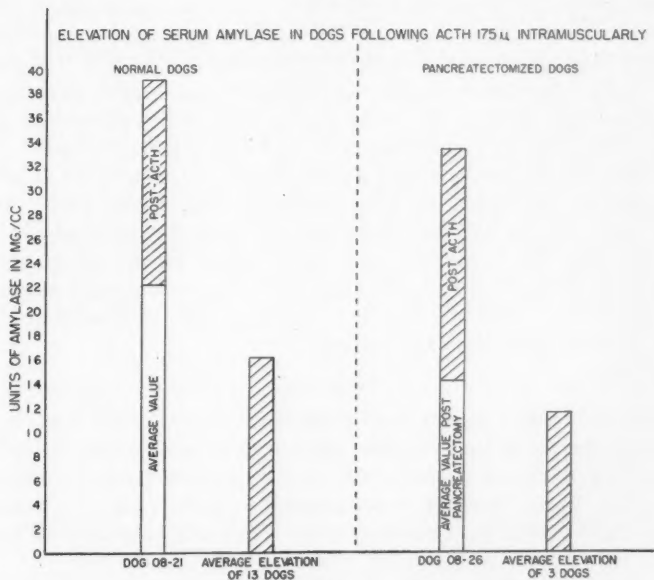


FIG. 5

significant in view of the fact that the ages ranged from 58 to 78 years: a range where good responses to stress would be less likely to occur.

DISCUSSION

The great variation in amylase activity found in the postoperative patient makes it difficult to conclude that a diagnosis of acute pancreatitis can be made

merely by amylase studies. In the first 2 groups, there was no patient who had an episode postoperatively that could in any way be construed as pancreatitis. Demerol and atropine were used preoperatively and demerol postoperatively.¹¹ In most instances of delayed rise in the amylase the patients were up and around, eating a normal diet. In addition, some of the greatest elevations of serum amylase were in cases having no relation to the pancreas and no evidence of pancreatitis at the time of the highest elevation. Examples are the 3 colon resections and 2 small bowel obstructions.

In the cases of little or no rise, and even of decreases from normal, there was a preponderance of biliary, gastric, and duodenal pathology. In several patients, there was definite trauma to the pancreas and in others there was disease closely associated with the pancreas, yet the amylase levels taken over a period of several days remained within normal limits.

The extra-abdominal cases lend further support to the hypotheses.

In the 27 patients who had a rise above 4 mg. per cc. two types of elevation were found. Ten of the patients showed an abrupt rise on the first postoperative day, with a rapid fall to normal in 48 hours. Seventeen patients had a delayed rise with a more prolonged elevation. The rise usually started on the third day, ascended to its greatest height on the sixth to seventh day, and then gradually declined to its preoperative level by approximately the twelfth day. These two curves were again found in the acute trauma cases which showed an increase, with 2 patients having an immediate rise and 3 having a delayed rise 4 to 6 days later. In the normal dogs receiving ACTH, 3 had immediate rises of the serum amylase and 10 had delayed increases 4 to 6 days later. Again in the pancreatectomized dogs receiving ACTH, 1 had an abrupt rise and 2 had delayed rises of 2 and 5 days later. When ACTH was administered to human beings, the serum amylase again became elevated either immediately or as a delayed response. The obvious correlation exhibited by these groups suggest that the amylase elevation was due to anterior pituitary hypertrophy.

SUMMARY

Evidence has been presented that elevations in serum amylase levels cannot be explained by disease of the pancreas except in so far as it is a nonspecific insult.

The amylase studies on dogs after ACTH were found to have a correlation with the elevation of serum amylase in postoperative patients. Also, the findings correlated with the elevation of serum amylase in patients suffering from traumatic injury.

In 5 out of 6 patients receiving a course of ACTH therapy, a definite elevation of serum amylase level was present.

The great variation of amylase activity found in patients suggests that there is no dependable relationship between elevations of the serum amylase and acute pancreatitis.

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SURGICAL CONSIDERATIONS IN THE TREATMENT OF PANCREATITIS*

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Pancreatitis, in its various manifestations, has been the subject of a vast amount of investigative work and numerous clinical studies. Despite this, we still lack adequate understanding of many features of this disease, particularly those relating to etiology and pathogenesis. The very multiplicity of proposed therapeutic attacks is eloquent testimony to the inadequacy or ineffectiveness of most of them, and the disease continues to be a scourge to its victims and a vexing and frustrating problem for those to whom these victims look for help.

Time does not permit a detailed account of the many ingenious and varied attempts to clarify and explain the various factors concerning pancreatitis. Many excellent discussions of the problem have been published, among them those of Opie,^{15, 16, 17} Archibald,^{1, 2} Gage and Floyd,¹³ Doubilet and Mulholland,⁹ Sensening and Bowers,¹⁹ and Whitrock, Hine, Crane and McCorkle.²¹ The monograph of Cattell and Warren⁸ contains a wealth of information about the various diseases of the pancreas, and includes bibliographic reference to most of the important papers on this subject. In this brief report, no attempt will be made to summarize further the many papers which have appeared: detailed references to works referred to in the body of the paper can be found in the above reviews, except as noted.

Among the many theories as to the pathogenesis of pancreatitis, certain ones stand out above the rest by virtue of the data which support them and the logic underlying their presentation. Chief among them are the following:

1. *The "Common Channel" Theory.* Opie, in 1901, noted the association of acute pancreatitis with a stone so impacted at the ampulla of Vater as to permit the reflux of bile into the pancreatic ducts through a cloacal type of joint entry of the biliary and pancreatic ducts into the duodenum.¹⁵ This stimulated many investigators to attempt the production of pancreatitis by various types of biliary injections into the ducts of the pancreas, and these were soon supplemented by the injection of numerous other substances at various pressures under a variety of experimental conditions. Others made careful anatomic studies in an effort to discover the frequency of a "common channel" which would permit biliary reflux into the pancreas should obstruction develop. While a considerable percentage of individuals do have such a ductal arrangement, it is beyond question that many others lack it, and still develop pancreatitis. It has been shown that bile injected into the pancreatic ducts does not produce inflammation unless it is injected at sufficient pressure to produce acinar rupture. It

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Presented during the twenty-fourth Annual Assembly of the Southeastern Surgical Congress, Richmond, Virginia, March 12-15, 1956.

also has been demonstrated that the secretory pressure within the pancreatic ducts is apt to be higher than that in the common duct (although these tend to equalize after cholecystectomy). All of these findings indicate that the common channel idea is by no means the complete answer as to the etiology of pancreatitis. Of particular interest in relation to reflux into the pancreas is the recent demonstration by photo-fluoroscopy that reflux from the *duodenum* into the pancreas can and does occur, even with separate entry of biliary and pancreatic ducts.⁷

2. *Obstruction.* It has been widely suspected that obstruction to the outflow of pancreatic secretions may be a major factor in the pathogenesis of this troublesome disease. Stone, spasm, edema and fibrosis at or near the duodenal papilla, and epithelial metaplasia within the ducts have been suggested as likely agents for the production of pancreatitis, in the presence or absence of associated biliary tract disease. Such obstruction has indeed been demonstrated repeatedly during the course of operations upon patients with recurrent pancreatitis, and the finding confirmed by radiographic ductography. The frequent finding of ductal dilatation in some of these patients is further, although indirect, evidence of ductal obstruction and many patients have experienced relief of their symptoms after procedures providing better drainage for pancreatic secretions.

On the other hand, it is well known that simple ductal ligation in the experimental animal uniformly produces atrophy of the pancreas, without pancreatitis, and it has been difficult to reconcile this fact with the idea of ductal obstruction as a major etiologic agent. Since recurrent pancreatitis is gradual in development, it occurred to us that more gradual occlusion of the pancreatic duct in the experimental animal might produce pancreatitis, in contrast to the simple atrophy caused by acute ligation. Utilizing one of the methods for gradual vascular occlusion developed by Berman,⁴ Drs. Floyd and Christophersen, working in our surgical research laboratories, have successfully produced pancreatitis in dogs.⁹² Subserosal injection of a fibrogenic substance, sodium dicetyl phosphate, into the wall of the pancreatic duct (which was then encased in a plastic collar to direct the fibrosis inward) caused the development of typical chronic pancreatitis in 8 of 9 dogs. The obstruction developed in about 4 months, and the pancreas of the animals, studied thereafter, showed typical pancreatitis histologically, with ductal dilatation, a feature commonly seen in human pancreatitis, but frequently missing in the disease as produced by usual experimental methods. Success of these experiments is evidence for gradual ductal occlusion as one of the factors in pathogenesis of pancreatitis. It also offers what may prove to be a valuable new experimental method for study of this disease.

3. *Other Theories.* Many other ideas have been advanced as to the etiologic basis for pancreatitis. Time does not permit an exhaustive discussion of these factors which may be found rather completely described in the material referred to above. Among these factors are infection (lymphogenous, hematogenous or by way of ductal reflux), circulatory disturbances, allergy, trauma, and alcoholism. The latter is particularly noteworthy because of the very frequent association of chronic alcoholism with chronic or relapsing pancreatitis. What the

relationship is it is difficult to say. Gage has suggested that patients with pancreatitis may well become chronic alcohol addicts in their frantic efforts to relieve themselves of pain. On the other hand, it is a well known fact that patients with relapsing pancreatitis are particularly prone to suffer an acute attack immediately subsequent to the ingestion of alcohol. Intravenous alcohol has failed to produce attacks in patients who develop them after oral intake, and it has been suggested that the effect may be based on a local and indirect stimulus to pancreatic secretion.¹⁰ This is but one of many problems which need further clarification.

Acute hemorrhagic pancreatitis: This disease, once considered an acute surgical emergency, is now generally accepted to be best treated by nonoperative measures, since the mortality rate following surgical exploration is significantly higher than that following nonoperative treatment. All of the therapeutic measures proposed and in use are aimed at rest of the patient and of his pancreas. These include bed-rest, gastric suction drainage, parenteral fluids only, paravertebral or epidural blocks for the relief of pain, and perhaps atropine or banthine in an attempt to cut down the volume of pancreatic secretion. Morphine probably should not be used because of its known tendency to produce spasm of the sphincter of Oddi; while demerol may have a similar effect, it is certainly not so great and it should be the analgesic agent of choice if the paravertebral blocks are not effective. Recent reports indicate that a carbonic anhydrase inhibitor ("Diamox") may materially reduce pancreatic secretion: this may provide an additional therapeutic procedure for treating the disease in its acute phase.^{5, 20} If laboratory studies indicate a marked calcium deficit, intravenous calcium gluconate should be administered for correction of this deficiency.

Chronic recurrent, or "relapsing" pancreatitis: The multiplicity of therapeutic attacks upon this condition has already been referred to. Priestley, Taylor and Rogers recently published a very comprehensive summary of the surgical methods which have been proposed.¹⁸ They present an excellent, simple classification:

- (1) Direct drainage of the biliary tract, either external or internal.
- (2) Procedures to decrease stimulation of pancreatic secretion.
- (3) Procedures to relieve spasm or other types of obstruction in the region of the sphincter of Oddi or terminal portion of the main pancreatic duct.
- (4) Direct operation on the pancreas.
- (5) Various operations on the nervous system used primarily for the relief of pain.

This classification will be followed in the following discussion.

Direct drainage of the biliary tract: Cholecystostomy and choledochostomy have been proposed in pancreatic disease because of the frequent association between biliary tract disease and that of the pancreas. Obviously, if stones are present, their removal will prevent obstruction at the sphincter of Oddi. There can be no quibbling about indications here, for the presence of stones or other biliary tract disease demand operative correction, with or without pancreatic disease; there is no effective "medical" treatment for gallstones or gallbladder disease. On the other hand, it has been suggested that cholecystostomy or choledochostomy

might improve pancreatic drainage by lowering pressures in the biliary system: it has not been proved that such will be the result, and in the absence of demonstrable biliary tract disease these operations must be considered of dubious value so far as effects upon the pancreas are concerned. If there is good evidence of a common channel, choledochojunostomy, as suggested by Bowers, should effectively eliminate reflux of bile into the pancreas.

Procedures to decrease stimulation of pancreatic secretion: Included under this heading are such operations as vagotomy (with or without gastroenterostomy) and gastric resection, the former aimed at reducing nervous secretory stimuli, the latter to reduce the hormonal effect. While there is logic behind their use, they have not been sufficiently effective in cutting down secretion to bring recovery, and most surgeons who have used them have reported disappointing results.

Procedures to relieve spasm or obstruction at the sphincter of Oddi: These operations usually are listed under the term "*sphincterotomy*", and many have been done transduodenally (with or without mucosal repair) and some by a "blind" technic, using a "*sphincterotome*". While there can be no argument against enlarging a demonstrably contracted or obstructed ductal orifice, the operation has been disappointing in our hands. Unless there be a common channel, it is difficult to see how enlargement of the orifice of the common bile duct could benefit the pancreas. The tendency for all surgically divided orifices to scar down to smaller size is well known, and we believe that mucosal repair should always be done. Even with this policy, however, we share the experience of many who have reported numerous cases of patients who had pancreatitis continue to have attacks despite sphincterotomy.

Direct operation on the pancreas itself: Retrograde pancreaticojejunostomy has been recommended recently as an effective method for draining the pancreas whose ductal system is obstructed at the duodenal end.^{3, 11, 22} DuVal has given a quite rigid set of criteria for justification of the employment of this procedure;¹¹ certainly his insistence that obstruction be demonstrated and that there be ductal dilatation is wise. Early reports indicate that good results have been achieved by a number of surgeons using this technic in properly selected cases. Our longest follow-up is a patient with recurrent pancreatitis upon whom we performed this operation some 2 years ago; she has remained well since, without recurrence of symptoms. The previously drained pseudocyst in the head of her pancreas which persisted (although reduced in size), despite cystogastrostomy, has now disappeared, and the patient looks and feels well. Retrograde pancreaticojejunostomy would appear to be an excellent procedure for the occasional patient with proper indications.

Elimination of the pancreas or its function would seem desirable, if we consider the attacks to be related to functional activity of the gland. Partial and even total pancreatectomy have been reported many times, and have been used as "*last resort*" measures for patients in whom all other therapeutic measures have failed, and whose disease continues to be incapacitating. Undoubtedly it can be justified in some instances, but the need for substitution therapy, and

particularly for control of the permanent diabetes produced by excision of the gland, must make this operation one of last resort. The desirability of elimination of the exocrine function of the pancreas while still preserving the endocrine activity suggests the possibility that simple ligation of the pancreatic ducts might achieve the desired result. The classic work of Banting and Best showed that islet function will persist after ligation of the ducts, and other experiments referred to earlier in the paper have indicated that atrophy of the gland, without pancreatitis, is produced by ligation of the ducts in the experimental animal. Martin and Canseco, in 1947, reported the first such operation we have found in the literature.¹⁴ A fourth year student suggested this procedure to them for the above mentioned reasons, during ward rounds, and Rienhoff performed the operation in March 1946, placing a series of silk sutures in the pancreas so as to occlude both main and accessory ducts. Their patient was relieved of pain, and was still well 10 months later, at the time of publication of the paper. The only other report of utilization of this procedure which we have found is that of Cannon in 1955.⁶ He reports ductal ligation in 6 patients, 4 of them carried out transduodenally, 2 extraduodenally. In every case the duct of Wirsung was ligated, but the duct of Santorini was probably left intact in 2 and possibly a third. The logic of the author's statement that both ducts should be ligated if complete atrophy is to be produced is inescapable. The results in this small series are quite variable, and not conclusive: 1 patient was clearly relieved, 2 were possibly benefited, 1 received no benefit from ligation of the duct of Wirsung only, 1 was too recent to evaluate at time of publication, and 1 died of pulmonary embolism. Despite these rather equivocal results, there appears to be such sound reasoning behind the procedure that further use of the ligation of both ducts in carefully selected cases would appear in order.

Two clinical cases which we have been following for some time emphasize the possible relief which pancreatic atrophy might offer:

CASE REPORTS

Case 1. L.W., a 27 year old Negro man was first seen on March 17, 1953, at which time he was diagnosed as having acute appendicitis. An appendectomy was performed and his postoperative course was uneventful. He was next seen in October, at which time the differential diagnosis lay between a penetrating ulcer and an acute pancreatitis. On his fourth admission, in December of 1953, he again presented rather typical findings of acute pancreatitis, but his amylase determination showed only 400 units. He was explored because of the possibility of a perforated duodenal ulcer. At the time of this exploration, the gallbladder was found to be greatly distended and tense, but it was thin-walled and of normal color and there were no stones palpable. The head of the pancreas was very large and hard and the entire body of the pancreas was swollen and edematous. A liver biopsy was performed, and a report of chronic, intrahepatic cholangitis was returned. He recovered uneventfully and was discharged. He was admitted for still another time on Feb. 6, 1954, with the same symptoms as previously, but his amylase was not over 400. He was readmitted in May 1954, still with the same symptoms. After the patient had become quiescent, a sphincterotomy was performed. The sphincter was identified, sectioned, and then the mucosa of the ampulla of Vater was sutured with interrupted fine silk to the mucosa of the duodenum. Exploration of the pancreas revealed that this time it was about one-half of its normal size, nodular, and only moderately hard. The body and tail of the pancreas were much atrophied and extremely hard and fixed.

From that time until August of 1955, the patient had 9 admissions to the hospital, with fairly classical symptoms of acute pancreatitis. The sphincterotomy obviously did not relieve him of his disease. During these admissions he was treated by nasogastric tube, atropine, splanchnic blocks, and fluids. It became apparent that these return admissions were getting closer together, although the severity and duration of his attacks were steadily diminishing. Our belief that he was gradually developing pancreatic atrophy was confirmed by a fasting blood sugar of 675 at this admission.

Following his bout of pancreatitis he was transferred to the medical service for control of his diabetes. He was discharged from the hospital on 70 units of U-40, NPH insulin.

His last admission was on Jan. 9, 1956, when he returned with the same rather classical symptoms of acute pancreatitis. At this time his blood sugar was 265 mg. per cent, and his serum amylase was 536. His attack of pancreatitis at this admission did not seem quite so severe, but control of the diabetes had become somewhat of a problem.

Case 2. D.F., a 24 year old Negro woman was first seen by the surgical service of this hospital in July of 1954. Her complaint at this time was a severe epigastric pain with an onset at approximately 2:00 p.m. on the evening prior to admission after drinking considerable beer at a picnic. Pain radiated through to her back to the subscapular regions bilaterally. She had vomited several times, and there was no history of any previous episode. Her abdomen was exquisitely tender to palpation and there was rebound tenderness throughout the entire abdomen. The differential diagnosis lay between duodenal ulcer, acute pancreatitis and possible acute gastritis. Her serum amylase at this time was 340 units. An upper gastrointestinal series showed no abnormality of esophagus, stomach, or duodenum. She was treated with splanchnic blocks, a nasogastric tube, and atropine, and was discharged on the twelfth hospital day.

She was readmitted in October and November 1954, and April of 1955 with the same complaints and was given the same treatment. She was admitted a month later with a little milder symptoms. After still another admission a month later, it was decided that she warranted exploration with the possibility of doing a retrograde pancreaticojejunostomy. The duodenum was found to be adherent to the gallbladder and the under surface of the liver. The stomach was grossly normal. The common duct was normal. The pancreas was found to be very dense, fibrous, and represented a string-like structure going superiorly and to the left across the upper abdomen in its normal relationship, and was approximately the size of a thumb. The head of the pancreas was likewise well contracted, firm, and non-adherent. It was decided that no operative treatment was indicated in view of the apparently fibrotic pancreas.

Since this time she has had 4 additional admissions to the hospital, each time with the same complaints and has been treated in the same manner. As yet she has shown no elevation in her blood sugar. Her attacks have progressively decreased in severity and in duration.

The course of these patients indicates that gradual pancreatic atrophy is taking place, presumably as a result of their disease. It is our hope that progressive atrophy eventually will result in elimination of the attacks of pancreatitis. We have not yet felt justified in trying to produce this effect by simple ligation of the pancreatic ducts; but we cannot escape the feeling that there may be more logic in this than in many of the other procedures now being used, often with little or no benefit to the patient.

Operations on the nervous system for relief of pain: Sympathectomy has been used for many years to relieve the severe pain in these patients. There is no proof, however, that this operation has any effect upon the disease itself, nor that it in any way influences the frequency or severity of the attacks. Further, there is some question as to the permanence of the pain relief. A few years ago, in Detroit, Dr. Alfred Large and I followed a number of patients with sympathect-

tomy for pain relief in recurrent pancreatitis. We thought the results were excellent and we became rather impressed with the procedure. However, in a matter of 2 or 3 years most of these patients were again complaining bitterly of their pain, and we lost much of our enthusiasm for the operation. Nevertheless, there can be no denying that these people are truly miserable, and even a year or 2 of pain relief may well justify the relatively minor risk of sympathectomy.

SUMMARY

Chronic relapsing pancreatitis is one of the most baffling and troublesome diseases confronting us. Of the many operative measures aimed at its relief, only a few offer promise. If there is biliary tract disease, it should be treated as such, rather than for possible benefit to the pancreatitis. If there is demonstrable obstruction at the duodenal papilla, sphincterotomy, under direct vision and with mucosal repair, will benefit biliary flow, and may help pancreatitis if there be a common channel. If attacks continue, or if there is no biliary tract disease, an attempt should be made to determine whether or not there is pancreatic ductal dilatation; if so, retrograde pancreatocoejunostomy offers considerable hope of benefit. If all other methods fail, consideration must be given to attempts to eliminate all exocrine function of the pancreas. Recently reported clinical experience, and logic, based upon much animal experimentation, indicate that consideration should be given to ligation of both pancreatic ducts as a means to this end, in the hope that acinar atrophy will result without loss of islet function. Finally, and only as a last resort, pancreatectomy may have to be resorted to, bearing in mind the inevitable permanent need thereafter for replacement of both endocrine and exocrine secretions of the pancreas.

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A STUDY IN POSTMENOPAUSAL UTERINE BLEEDING

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The symptom of uterine bleeding 12 or more months after cessation of normal menses has been the subject of many reports. Most authors report a high incidence of genital-tract malignancy, varying from 16 per cent of McFadyen⁴ to 87 per cent as reported by Zweifel.⁸ Emphasis usually has been on the incidence of malignancy. Until the last few years most reports have included cases of postmenopausal bleeding from sites other than the uterus. Recent studies,^{1,2} as this one, including only patients bleeding from the uterus, have found in nearly two-thirds of all cases adequately investigated that malignancy was not the cause of this abnormal bleeding. In half of the nonmalignant cases no cause for the bleeding could be demonstrated. The frequent finding of concomitant constitutional disease, such as obesity, hypertensive-cardiovascular, renal, and liver diseases, and diabetes, is the rule in this age group and frequently classifies the patient as a less than desired surgical risk.

The purpose of this study is twofold: First, to learn by follow-up examination what happens to the nonmalignant group; how many have recurrence of bleeding; how many develop cancer later or have it unrecognized at initial examination—and second, to consider what is the role of surgery in managing patients with nonmalignant postmenopausal uterine bleeding.

Materials

The records of all patients with uterine bleeding one or more years after the menopause for the years 1950–54 inclusive were studied. The establishment of the uterus as source of bleeding was by finding blood in the cervical and/or vaginal canals at examination with the exclusion of vaginal or external genital lesions as the source. Also, the history of daily bleeding from the genital tract with amounts requiring several pads, with no lower genital tract lesion present, was accepted as uterine bleeding. All patients with this symptom were studied in the University Hospital. This 1950–54 group of patients were selected because they meet the requirements of our investigation routine indicated in table 1. When there was recurrence of bleeding the study-routine was repeated regardless of the bleeding site. Table 2 indicates our explanation of bleeding after the initial investigation.

A comparison with this report of recent reports on postmenopausal bleeding from the uterus is made in table 3. It will be noted in the averages that malignancy was found in slightly more than 30 per cent of the patients while bleeding from nonmalignant reasons accounted for nearly 70 per cent. This is a greater

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Presented during the Richmond Assembly of The Southeastern Surgical Congress, March 12–15, 1956, Richmond, Virginia.

TABLE 1
Routine investigational procedure

- A. Hospitalization.
- B. History and physical—Laboratory Data. Careful evaluation as surgical risk.
- C. Cyto Smears for presence of tumor cells. Originally, and at periodic follow-up.
- D. Cervical dilatation and cervical biopsies. Fractional curettage or coring.
- E. Bimanual palpation under anesthesia for uterine and adnexal disease.

TABLE 2
Postmenopausal uterine bleeding
1950-54

Data	No. Patients	Per cent
Malignant lesions.....	46	30.26
Nonmalignant lesions.....	47	30.92
Cause not demonstrated.....	59	38.82
Total.....	152	100.00

TABLE 3
Postmenopausal uterine bleeding
(Comparison of reported studies)

Author	Year	Total Cases	Malignancies	Benign Lesions	Cause Undetermined
Brewer-Miller	1954	211	58—27.5%	72—34.1%	81—38.4%
Baldwin-Jacobs	1955	122	46—37.7%	41—33.7%	35—28.6%
Present	1956	152	46—30.26%	47—30.92%	59—38.82%
Average.....			30.94	32.98	36.09

incidence of postmenopausal uterine bleeding—not due to cancer—than reported when all sites of bleeding are included. Moreover, the group in which the cause of bleeding was not determined is the largest—whereas in the earlier reports this group accounted for less than 10 per cent of all patients with this symptom.

Nonmalignant Cases

Our conclusions as to cause of bleeding in this group are found in table 4. They do not differ significantly from recent reports. The mechanism of bleeding in uterine polyps, submucous myomas, and cervical infection with ulceration and/or stenosis with pyometra require no explanation. In hyperplasia of endometrium one has to choose between the explanation of Novak,⁵ Speert,⁷ and Gianaroli³ as to how bleeding occurs. We can add to none of these. However, we are impressed by Gianaroli's concept of bleeding from vessel dilatation or vessel telangiectasia in the endometrium. This author found such vessel changes in a high incidence of uteri that showed either endometrial atrophy or "no endometrium"

TABLE 4
Postmenopausal uterine bleeding
 1950-1954

<i>Non-malignant causes:</i>	
A. Benign lesions:	
1—Polyps (E-15, C-9)	24
2—Hyperplasia	11
3—Cervical laceration	9
4—Submucous myoma	2
5—Papillary serous cystoma	1
	47
B. Cause undetermined	59
Total	106 Cases

at curettage. Brewer and Miller² found that the amount and duration of bleeding may vary widely from spotting to flooding and was of no significance as to cause.

Follow-up of Non-Malignant Cases

One hundred and one of the 106 patients were followed until Feb. 1, 1956. Only 5 could not be followed. Two patients had benign lesions originally as cause of bleeding and 3 had no demonstrable cause. Other than data of original work-up no information is known on these 5 patients since they did not return for examination as requested. However, relatives reported that one patient died of pulmonary disease without recurrence of bleeding.

The objective of follow-up visits (every 4 to 6 months) was to learn if bleeding reoccurred and what was the cause. We were anxious to know if we had missed malignancy on initial study, or if it developed later. At each visit the history was reviewed, the patient was re-examined—taking slide smears for cytology study and biopsies when indicated. The last follow-ups of 101 patients were in November–December 1955 and January 1956.

It will be noted in table 5 that out of 101 patients followed, 47 for more than 3 years, that only 18 had recurrence of postmenopausal bleeding. Only 1 patient with recurrent bleeding of the 101 followed was found to have cancer. This was adenocarcinoma of the endometrium. It is not known whether this case represents

TABLE 5
Postmenopausal uterine bleeding
 (Five year study—non-malignant cases)

Data	No. Cases	Follow-up	Recurrent Bleeding	Cancer Found
Benign lesions	47	45 (95.8%)	9	1
Cause undetermined	59	56 (94.9%)	9	0
Total	106	101	18	1

TABLE 6
Postmenopausal uterine bleeding
 (Non-malignant cases—follow-up)

Year	No. Cases	Follow-up	Recurrence	Cancer Found	Hysterectomy
1950	17	16	4	0	1
1951	14	14	1	0	1
1952	18	17	4	0	0
1953	29	27	6	0	1
1954	28	27	3	1	1
Total	106	101	18	1	4

missed diagnosis at first curetting or development of endometrial neoplasia in a uterus containing myomas and polypi. Malignancy was found 14 months later at curettage after finding of a Grade Four positive cytosmear. Bleeding had reoccurred 4 months earlier. Hysterectomy was not done until bleeding reoccurred and malignancy was found, because the patient was considered not too good a surgical risk on basis of obesity and hypertensive cardiovascular disease. Her blood pressure was 238/140. The surgical specimen showed minimal myometrial invasion.

Cancer was not found in the 56 patients followed in whom no cause was determined for bleeding even though 9 had the symptom to reoccur. One would not project a probable incidence of cancer development in a group of uteri containing benign lesions or containing no demonstrable lesions because the impact of constitutional disease is not known nor has such a group had a follow-up to death.

Systemic Disease in Non-Malignant Cases of Postmenopausal Bleeding

It was surprising to note in table 7 that almost half of this group was found to have systemic disease. Hypertensive cardiovascular disease was the most common, with diabetes mellitus next. The diagnosis of hypertensive cardiovascular disease was made on basis of blood pressure readings of 160/96 or above, cardiac hypertrophy, electrocardiographic changes, and retinal vessel studies. If a patient was considered less than desired surgical risk because of systemic disease, an

TABLE 7
Postmenopausal uterine bleeding
 Systemic disease in non-malignant group

	Benign Lesions (47)	Cause Undetermined (59)	Total—106
HCVD.....	18	18	36
Diabetes.....	5	3	8
Syphilis.....	2	1	3
Misc.....	1	4	5
Total.....	26 (55.3%)	26 (44.1%)	52 (49.05%)

evaluation was made in each instance by Staff Members of Department of Medicine in the Medical College of Alabama. In this group of 106 patients, 52 had constitutional disease and 17 severe enough to be classified as very poor surgical risks.

Unquestionably major surgery is a poor therapy choice in many patients with postmenopausal uterine bleeding which was found not to be due to cancer on first or second investigation. This study finds the poor risk incidence of 15 to 17 per cent and the cancer development incidence after negative findings at second investigation much less than 5 per cent in admittedly a short follow-up. However, one would expect systemic disease rate and toll to increase over cancer incidence as this same group of patients is followed.

The Role of Surgery for Nonmalignant Postmenopausal Bleeding

In our opinion the application of major surgery as a therapy method in this group must be considered in the light of observed neoplasia development incidence, which is quite low, as against systemic disease incidence and poor surgical risk, which is high. We believe that in moderately advanced systemic disease, hysterectomy with special pre and postoperative care could well be a greater hazard than the potential development of cancer. Following a rule of procedure should not be acceptable.

In the good and fairly good risk-patients, curative surgery—e.g., hysterectomy, is advocated after the second complete diagnostic study in the following conditions:

1. When pelvic benign lesions or vaginal herniations per se require surgical correction.

TABLE 8
Benign lesions
(Recurrent bleeding)

Case	Year	First Investigative DX	Second Investigative DX	Year	Final RX	No Recurrence
1	1950	E. Polyp— HCVD	E. Polyp— HCVD	1951	Radium	0
2	1952	E. Polyp	E. Polyp—Ul- cerative Cer- vicitis	1952	Abd. T. Hyst.	0
3	1952	Cx Ulcer	Cx Ulcer	1953	Coring Cx	0
4	1952	Cx Ulceration	Cx Ulceration	1952	Coring	0
5	1953	E. Polyp	E. Polyp	1953	Abd. T. Hyst.	0
6	1953	E. Polyp	Atrophic Vagi- nitis	1954	None	0
7	1954	E. Polyp	E. Polyp	1955	Abd. T. Hyst.	0
8	1954	E. Hyperplasia	E. Hyperplasia	1954	None	0
9	1954	E. Polyp— Myoma— HCVD	(E. Polyp— Myoma— HCVD Endo- metrial Ca.)	1955	Abd. T. Hyst.	0

TABLE 9
Recurrent bleeding
 (Cause not demonstrated)

Case	Year	First Study Diagnosis	Second Study Diagnosis	Year	Final RX	Recurrence
1	1950	Chr. cervicitis atrophic end.	HCVD	1954	0	0
2	1950	Chr. cervicitis atrophic end.	Chr. cervicitis	1954	0	Lost—no follow-up
3	1950	Chr. cervicitis atrophic end.	Chr. cervicitis atrophic end.	1951	0	0
4	1951	Atrophic end.— HCVD lues	Chr. cervicitis atrophic end.— HCVD	1952	0	0
5	1952	HCVD—chr. cervi- citis No endometrium	HCVD—chr. cervi- citis No endometrium	1952	0	0
6	1953—46,	Atrophic end.	Ulcerative cervici- tis	1954	0	0
7	1953—60,	No end.— HCVD	HCVD—no end.	1954	0	0
8	1953—67,	No. endometrium	Chr. cervicitis	1954	0	0
9	1953—48,	No. endometrium	Chr. cervicitis	1954	Cx Coring	No follow- up

Note:—One patient lost in follow-up—All others examined and had Cyto Smears—January 1956.

2. When endometrial polyp or atypical endometrial hyperplasia is found at second curetting.

3. When postmenopausal uterine bleeding reoccurs in the patient with diabetes. Palmer⁶ reported endometrial carcinoma 10 times more common in the diabetic patient.

4. When pelvic examination or culdoscopy under anesthesia can not exclude adnexal pathology.

5. When cancerphobia becomes a paramount psychic problem in spite of reassurance.

In the 106 patients whose cases were not diagnosed as a malignancy, 4 hysterectomies were done, all after recurrent bleeding and second investigation. Two for recurrent or persistent endometrial polyp and one for endometrial polyp and cervicitis. One for endometrial carcinoma and polyp with myoma.

Intracavitary radium was used once in 1950 for a patient with recurrent bleeding, endometrial polyp, and hypertensive cardiovascular disease. A cerebral vascular accident had occurred between investigations. Bleeding has not occurred after irradiation.

We would not advocate hysterectomy for endometrial hyperplasia found repeatedly at curettage unless it was considered atypical in the absence of possible exogenous hormones. Pathologists are not uniform in classifying endometrial hyperplasia and clinicians are not in accord as to its significance.

SUMMARY

A study of all patients, including follow-up, presenting the symptom, postmenopausal uterine bleeding has been made for a 5 year period 1950-54.

In 152 patients, genital tract malignancy was the cause in 46 (30.26 per cent), benign lesions in 47 (30.92 per cent) and the cause was not demonstrated in 59 (38.82 per cent) patients. The total nonmalignant cause of this symptom was 106 or 69.73 per cent.

Of the 106 patients found not to have malignancy at initial diagnostic survey, 101 (95.28 per cent) have been followed 6 or less years. Only one patient developed malignancy later or had it and was not diagnosed at initial study.

Of the 106 patients in the nonmalignant group 52 (49.11 per cent) were found to have moderately advanced to advanced constitutional disease. Eighteen (16.9 per cent) patients were classed as poor surgical risks.

The role of hysterectomy or curative surgery has been discussed.

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CYSTIC DISEASE OF THE BREAST

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When operating upon patients with benign lesions of the breast, how often do we consider whether or not this particular breast is the seat of a lesion that might predispose to the development of a malignant tumor? With so much study being directed to the early detection of cancer, our every effort should be exerted to clarify, if possible, the still confusing problem of the association of cystic disease of the breast and cancer. This latter lesion is associated almost exclusively with the female breast but is seen in the male breast in the proportion of about 1:100.

I believe we can say with reasonable assurance that cancer for the most part occurs in a breast which is the seat of cystic disease and arises as such in the proliferative changes associated with cystic disease. This paper is concerned with a statistical study of 297 cases of carcinoma of the breast and 248 cases of cystic disease of the breast of patients who were operated upon at Mercy Hospital in Baltimore, Maryland, from 1941 to 1955.

A disturbing factor in any such study is the existence of a complicated and confusing terminology. Terms, all meant to convey the same idea, clutter the literature. They serve no real purpose and much confusion has resulted from their use.

One pitfall is the unfortunate use of the term chronic cystic mastitis and its use seems impossible of eradication. Foote and Stewart have called its persistent use a surgico-pathologic reflex. They dislike the term as it conveys no indication of the presence or absence of many characteristic histo-pathologic changes noted in such breasts. The chief objection, as we see it and as emphasized by Cheatle and Cutler,⁴ is that it includes a group of cases that are not hyperplastic or precancerous and require no specific therapy. The mazoplasias of Cheatle and Cutler, the mastopathies of Whitehouse, the generalized noncystic lobular hyperplasias of R. P. Smith,¹⁵ the nonencapsulated fibroadenoma, generalized adenomatosis, interacinar fibrosis and interstitial mastitis are some of the terms used to describe this particular group. The histologic changes are chiefly a piling up of epithelium in the ducts and acini, without cyst formation, and an increase in the periductal and periacinar connective tissue.

Ducuing⁵ described them as hyperplastic mastoses, characterized by microscopic multiple adenomas which as he stated "do not disturb the surgeon at all". He stated further that "they result in suspicion of cancer but the uniform configuration of the cells and the typical relations of nucleus and plasma stress their innocent character".

Presented during the Richmond Assembly of The Southeastern Surgical Congress, Richmond, Virginia, March 12-15, 1956.

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Thanks are due Dr. Leonard H. Flax who contributed greatly in assembling the statistical data appearing in this article.

To interpret some complaints, we should possess a knowledge of the normal physiology in order to determine whether the complaints are physiologic or pathologic. Normally, the breast is under the control of the hormones. In the normal cycle the breast continuously undergoes, from puberty to menopause, proliferative or hyperplastic and regressive or involutional changes. Frantz⁸ believed that all the lesions grouped under cystic disease of the breast are probably hormonally induced even if they appear for the first time after the menopause.

The normal rhythmic cycle can be interrupted by hormonal imbalance with resultant excessive epithelial and connective tissue activity. We all have noted the hormonal influence in the relationship of benign mammary disease to cancer, chiefly the group of lesions designated as cystic disease.

Opposed to the above group are the cystic lesions of the breast which are proliferative, hyperplastic and progressive, and are in our opinion potentially cancerous. Probably, it could be said better that a breast, because of some stimulus—whether hereditary, hormonal or intrinsic—is the seat of cystic disease and is, because of the same stimulus, a likely seat of cancer and as such must be treated as a precancerous or potentially cancerous breast. In other words, because of the not infrequent development of carcinoma in a breast already the seat of cystic disease, there must be some common denominator that associates the two.

Experiments with mice and rats have shown that cancer can be produced by estrogenic stimulation. Geschickter⁹ has shown that cyst formation may occur in rats in response to intensive estrogenic stimulation. As Lewison¹² has stated, "the development of gynecomastia with proliferation of all epithelial elements which occurs following prolonged estrogen administration in prostatic cancer is highly suggestive of specific target organ tissue growth".

We include under the heading of cystic disease of the breast the following:

1. Cysts—solitary or multiple.
2. Hyaline stroma. The matrix around the acini shows an unusual number of hyaline connective tissue cells. The ducts are enlarged and their epithelium hyperplastic.
3. Cystic dilatation of ducts and acini.
4. Intraductal and intracystic papillomata.

(Sir Leathal Cheate³ has shown convincingly that dilatation of the duct system of a lobe of the breast is a frequent prelude to the formation of papillomas within the cysts which are formed.) He has traced all the stages of the process up to infiltration, permeation, and obvious carcinoma. One must accept his conclusion that most carcinomas of the breast originate within the ducts and not from the acini and that these changes are particularly likely to occur in the cystic forms of the disease. Of our 297 cases, 194 were designated as arising from duct epithelium.

One other similar observation should be made, although there is some controversy concerning it, and that is that large cysts are acinar in origin, are lined with flattened epithelium and probably are incapable of malignant transformation. The blue-domed cyst of Bloodgood¹ is typical of such a lesion and could possibly

explain Bloodgood's insistence that chronic cystic mastitis, as he used the term, was decidedly not a precancerous lesion.

Foote and Stewart⁷ state—"we can confidently say that we have seen cancer begin in duct papillomatosis, solitary and multiple cysts, apocrine epithelium and blunt duct adenosis—all counterparts of cystic disease of the breast".

Cheatle and Cutler⁴ showed histologically a progression of noncystic hyperplasia to cyst formation to neoplasia or papilloma and later carcinoma. Campbell² and Ewing⁶ have made similar observations.

Extensive clinical and statistical evidence exists to show a definite relationship between cystic disease of the breast and cancer. Campbell² concluded that cystic disease is frequently found in association with frank carcinoma and that various gradations of epithelial proliferation may exist to give the impression that cystic disease represents a progressive evolution of epithelial hyperplasia eventuating in carcinoma. Schimmelbusch's classic description of his nonencapsulated cyst-adenomatous type of cystic disease and his insistence that the lesion was neoplastic is considered as such to this day, and the treatment he advised, mastectomy, is still the proper therapy. One constant observation made by us in all breasts, the seat of cystic disease, is the presence of nests of cells resembling sweat glands and designated by some as apocrine epithelium.

We studied 248 cases of cystic disease. Of these, 115 patients were subjected to simple mastectomy and 25 were not operated upon. Of the remaining 108 patients, a total of 195 conservative excisions were done. Thirteen or 12 per cent later developed carcinoma, 8 occurring in breasts the seat of cysts, solitary or multiple, and 5 in lesions stated as intraductal papillomas. Bilateral lesions were found in 26 of the 248 patients. Married patients numbered 180 and single 68. The average age was 38.8 years (table I).

Of 297 cases of carcinoma studied by us, all were critically reviewed by our pathologist, Dr. C. Gardner Warner. After careful study, 268 or 90.2 per cent showed cystic disease of the breast associated with the carcinoma (table II). It is interesting to compare the average age incidence of the breasts with cystic disease and those with cancer of the breast. Our figures are compared with those of Foote and Stewart⁷ in table III.

Greenough and Simmons¹⁰ followed a group of 83 cases of women who had

TABLE I
Cystic disease of the breast

Number of cases	248
Married	180
Single	68
Not operated upon	25
Number of excisions	195
Simple mastectomy	115
Bilateral lesions	26
Average age	38

TABLE II
Microscopic description of cystic disease associated with carcinoma

Description	Number of Cases	Percentage
Solitary or multiple cysts	22	7.4
Hyaline stroma	82	27.6
Cystic dilatation and dilated ducts	119	40.9
Intraductal papillomas	38	12.8
Intracystic papillomas	7	2.4
Interacinar fibrosis	3	1.0
Unclassified microscopically	26	8.8
Total	297	100.00%

TABLE III

Author	No. of Cases of Cancer	Cysts or Cystic Dilatation		Papillomas		Total %	Average Age	
							Cystic Disease	Cancer
Foote and Stewart	300	82	27%	108	36%	63	41	48
Pessagno	297	141	47.5%	45	15.2%	62.7	38.8	55.2

local excisions for cystic disease for from 1 to 17 years. In 4.8 per cent of these patients, carcinoma of the breast subsequently developed.

Wammock¹⁶ reviewed 179 cases of cystic disease of the breast and 41 were recorded as borderline cases as evidenced by proliferative changes with invasive features.

Warren¹⁷ made an excellent statistical follow-up study of 1206 cases of cystic disease of the breast along similar lines, comparing the cancer incidence in cystic disease of the breast with the cancer incidence of the Massachusetts general female population. The follow-up ranged from 5 to 21 years. In the cystic group, 42 later developed cancer. In calculating the age group rates, the author concluded that the breast cancer attack rate for women with chronic mastitis and related lesions in the age group of 30-49 years is 11.7 times the rate for the Massachusetts female population in general. In the group over 50 years of age, it was 2.5 times as great and in the entire group 4.5 times as great. From this it can be seen that cancer is particularly prevalent in women under 50 and that hormonal stimulation must be considered a factor.

(Foote and Stewart⁷ in a review of 300 cancerous breasts found 82 or 27 per cent containing cysts. They stated further that the average age of benign cysts was 41, whereas in the cystic breasts with cancer the average age was 48. They stated also that of 1200 patients operated upon for cancer, 2.4 per cent had previous operations for benign breast lesions. Of 200 patients with cystic disease without cancer, 58 or 29 per cent showed duct papillomatosis. In the 300 patients with cancer, there were 108 or 36 per cent who had duct papillomatosis. In summary, 63 per cent of the patients with cancer had either cysts or papillomas.)

TABLE IV

Comparative figures of local excisions for benign cystic disease and number later developing carcinoma

Author	Local Excisions	Carcinoma
Greenough & Simmons	83	4.8%
Geschiekter	54	5.5%
Kilgore	57	10.0%
Pessagno	108	12.0%

In a study of our 297 cases of cancer of the breast, 186 or 62 per cent of the patients showed similar lesions (table III).

Geschiekter,⁹ in a review of 54 patients with local excisions, found that 3 or 5.5 per cent later developed cancer. Kilgore and associates¹¹ reviewed 103 patients with bloody discharge from the nipple. Six or 6 per cent had cancer without a palpable mass, 11 or 10 per cent had a palpable mass, a total of 17 patients. Of the 57 patients who had a local excision, 6 or 10 per cent developed cancer in the same breast within 2 to 5 years (table IV).

Of the 297 patients operated upon by us for cancer of the breast, 10 or 3 per cent had previous conservative excisions for cystic disease and at the time of the radical mastectomy 3 of the 10 patients had metastases. The average lapsed time between the conservative excision and the radical mastectomy was 6 years. The shortest time was 2 months and the longest 20 years. The average age at the time of the conservative surgery was 44 and the average age at the time of radical procedure was 50 years. The following is a typical experience.

CASE REPORTS

Case 1. A 39 year old white married woman was first admitted to Mercy Hospital on Feb. 4, 1955, with a large hard mass in the lower outer quadrant of the right breast associated with nipple deviation and axillary lymphadenopathy. A smaller, freely movable, apparently encapsulated, cystic mass was found in the upper outer quadrant of the left breast. Admission chest roentgenogram was negative. Conservative excision of the mass in the left breast was done. The pathologic diagnosis was cystic disease. A right radical mastectomy was done and the pathologic diagnosis was carcinoma simplex with axillary metastases. Approximately 9 months later, this patient returned with a mass in the left breast in the area of the previous excision with palpable axillary glands. The preoperative impression was carcinoma. A left radical mastectomy was done and the pathologic diagnosis was carcinoma simplex with axillary metastases.

In addition to the 10 patients who had previous local excisions, 12 had either refused surgery when first seen or when told by their local physicians that surgery was not indicated with such comments as "you have nothing to worry about, it's just a tiny cyst". One patient was told she had a "milk vein". In all, 6 were advised surgery was not necessary and they had nothing to worry about. Five refused surgery. One patient was advised by her physician that she had a cyst and was given x-ray treatments in his office. One year later she was operated

upon for carcinoma of the breast with axillary metastases. One of the patients who refused surgery was told she had a breast which needed careful watching and she should return in 3 months for a thorough check. She was not seen again until 2 years later when she presented herself with the classical clinical picture of carcinoma of the breast for which a radical mastectomy was done. The pathologic diagnosis was adenocarcinoma with axillary metastases. Average delay in the institution of proper therapy in these 12 patients was 4 years.

Four of the group who had previous simple mastectomies of one breast for cystic disease developed carcinoma in the remaining breast. The following case is an example.

Case 2. A white married woman, aged 43, was first admitted to Mercy Hospital on July 23, 1950, with a "lump" in her left breast which she first noticed 2 weeks before admission. Examination revealed multiple, discrete, freely movable, apparently encapsulated, cystic masses of varying sizes in the left breast. Examination of the right breast was negative. Two days following admission, the patient was taken to the operating room and a left simple mastectomy was done. The pathologic diagnosis was "fibrocystic disease with blue-domed cyst". Eight months later, the patient returned with a "lump" in her right breast of approximately 4 weeks duration. Examination revealed a discrete, freely movable, nontender mass in the upper outer quadrant of the right breast. On April 14, 1951, the patient was operated upon and a right simple mastectomy was done. The pathologic diagnosis was "chronic fibrocystic disease of the right breast with early preinvasive carcinoma".

In solitary cysts, as demonstrated by clinical examination, the proper procedure depends upon several factors including the age and wishes of the patient. We believe that it is rare for any breast to be the seat of only one cyst and in acceding to the patient's wish and doing a local excision, we often have noted that we have left pathology. In other words, behind a simple excision there is a diffuse process. If a local excision is the procedure, the strictest postoperative observation is indicated. In those patients over 40 years of age, simple mastectomy is the procedure of choice. If cystic disease is localized and the patient is under 40 years of age and the woman is desirous of keeping her breast, a local excision is done. If another cyst follows that, a simple mastectomy should be advised or a radical mastectomy if cancer is demonstrated. The following case is worthy of note.

Case 3. A 32 year old white single woman was first admitted to Mercy Hospital on Nov. 2, 1950, with a lump in the inner quadrant of her left breast of approximately 2 weeks duration. This mass was very smooth, apparently encapsulated, nontender, freely movable. Simple excision was done. The pathologic diagnosis was fibrocystic disease of the left breast with blue-domed cyst. The patient was asymptomatic until 4 years later when she was again admitted on Nov. 4, 1954, with 2 similar discrete masses in the upper quadrant of the left breast. These masses again were freely movable, nontender, and apparently encapsulated. It was the patient's wish that we be conservative and accordingly these masses were excised and the pathologic diagnosis was "cystic disease with blue-domed cyst". Approximately 9 months later, this patient was readmitted with a similar cystic mass in the upper outer quadrant of her left breast. A simple mastectomy was advised but the patient again refused and a local excision was done. The pathologic diagnosis was "fibrocystic disease with blue-domed cyst".

I am sure we must agree that this patient has a potentially malignant breast which demands careful watching.

(We believe that women 40 years of age or above, with a bloody discharge from the nipple, with or without a palpable tumor, or even localization by segmental milking, should be advised to submit to simple mastectomy as these lesions more often than not are multiple and prone to malignant degeneration. If cancer is demonstrated then the radical operation is proceeded with. In the young, if the lesion is localized, segmental excision can be done with careful postoperative observation. If multiple papillomas are demonstrated then simple mastectomy is the procedure of choice at any age.) We cannot as of now, in cystic disease, determine which breasts will develop cancer and which will not.

Delay in the institution of appropriate therapy results in the loss of life in many patients who would otherwise be saved.

Just a word concerning aspiration in the therapy of cystic disease of the breast. Patey and Nurick¹³ recorded their experience with 76 patients treated conservatively by aspiration. Sixty-five were followed from 1 to 16 years. Only one is known to have developed carcinoma and that in the opposite breast. They stated that aspiration is an efficient and safe treatment for cystic disease of the breast. We do not agree with their conclusions nor do we believe that aspiration with centrifuging of the aspirated fluid is an adequate method of diagnosis as the following case will attest.

Case 4. A 43 year old white woman presented herself to another surgeon with a cystic lesion of the right breast. Aspiration with centrifuging of the aspirated fluid revealed no tumor cells and she was told no further treatment was necessary. She was seen by us 7 months later at which time the right breast was tender, indurated, and exhibited the classical signs of carcinoma. A right radical mastectomy was done and the pathologic diagnosis was scirrhous carcinoma with axillary metastases.

SUMMARY

It is believed that cystic disease of the breast which includes in addition to cysts—solitary or multiple—intracystic or intraductal papillomas, hyaline stroma, and cystic dilatation of ducts and acini can be in direct etiologic association with cancer. We believe further that statistical and histologic studies as well as clinical experience confirm this conclusion.

We consider that it is useless to attempt to classify accurately benign breast lesions on a purely histologic basis. The use of the term chronic cystic mastitis should be discouraged. A better understanding of the problem would be possible if we kept in mind two separate groups: the hyperplastic noncystic group which is definitely not precancerous and the cystic lesions which definitely predispose to the development of cancer.

In a critical review of 297 cases of carcinoma of the breast, 268 or 90.2 per cent showed associated changes characteristic of cystic disease. Of these 297 cases 194 were designated as arising from duct epithelium. Ten or 3 per cent of these patients had previous conservative excisions for cystic disease and at the time of the radical procedure, 3 of the 10 had axillary metastases.

In 12 additional patients whose cases were diagnosed as cystic disease when first seen, 5 refused surgery, 6 were advised by their local physicians that surgery was not indicated and one was given "x-ray therapy" in the physician's office.

The average delay in the institution of proper therapy in these 12 patients was 4 years.

Of 248 cases of cystic disease studied by us, 115 patients were subjected to simple mastectomy, 25 were not operated upon. Of the remaining 108 patients, a total of 195 conservative excisions were done. Thirteen or 12 per cent later developed carcinoma, 8 occurring in breasts the seat of cysts and 5 in lesions stated as intraductal papillomas.

In the surgical management of cystic lesions of the breast, we believe that simple mastectomy is the procedure of choice in women over 40 years of age. If under 40 years of age, and the lesion is localized, conservative excision can be done with careful postoperative observation. In breasts the seat of papillomas, as evidenced by bloody discharge from the nipple, a simple mastectomy should be the procedure after 40 or at any age if multiple. If localized, in the young, then local excision with careful postoperative observation may be the choice.

The procedure of aspiration and centrifuging of the fluid in the cysts in the treatment or diagnosis of cystic lesions of the breast should be discouraged.

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DIVERTICULA OF THE FEMALE URETHRA

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Diverticulum of the female urethra may be defined as a sacular dilatation of a circumscribed area nearly always below and communicating with, the floor of the urethra. It usually is under the middle or distal portion of the urethra (fig. 1), but may dissect well posterior beneath the trigone (fig. 2). The sac may even encircle the urethra. The opening can be single or multiple (fig. 3), narrow or wide.

One day during the past year my attention was pointedly drawn to the frequency of their occurrence, even though the literature treats them as a rarity. Our clinic was visited by surgical representatives of a Mid-Western group. The remark was made, "you have the opportunity to see many of these cases being in a large center and being connected with a woman's medical school, while we never see this condition." This statement caused me to think about the matter. I found that only one-half of my cases came from the latter source while the others came from a general urologic practice, patients referred from practitioners in the surrounding areas.

It is interesting to note that O'Brien and Mitchell¹⁴ in a discussion of chronic bladder irritation in females, never mention a case of diverticulum of the female urethra. They review 200 cases where the diagnoses ranged from chronic urethritis and trigonitis, kidney and ureteral stones, acute and chronic pyelonephritis, all the way to hydronephrosis and stress incontinence. It seems unbelievable from our experience that such could be so when in 74.5 per cent of their cases, "symptoms resulted from primary disease of the urethra and trigone".

The experience showing the wisdom and importance of calling this condition to the attention of medical and surgical groups is very aptly summarized by Gilbert and Cintrón.⁵ They make note of the fact the condition was diagnosed only 30 times at Johns Hopkins Hospital¹⁷ from 1890 to 1940; only 7 cases were seen at the Cleveland Clinic⁷ in 22 years and 71 cases reported at the Mayo Clinic² as of 1948. In their local hospitals in Puerto Rico no cases had been reported until after Carson¹ read his paper on this condition before their hospital staffs in 1950. Following this, several cases were reported rather quickly. Johnson¹¹ reports a similar experience at the University of California when only 2 cases were recorded up to 1930. Following the demonstration of 2 cases, 9 additional cases were recognized in one year.

ETIOLOGY

No doubt most of the diverticula are acquired as the result of trauma secondary to parturition, catheterization, urethral stricture, urethral stone and intraurethral therapy. However, it seems to be most logical, that many are secondary to

Presented during the Richmond Assembly of The Southeastern Surgical Congress, March 12-15, 1956, Richmond, Va.



FIG. 1. Showing the diverticulum well distal toward the external urethral meatus

intramural infection with resultant abscess formation. The presence and character of the periurethral glands in the female⁸ seems to make this logical. The urethritis so often seen in the female is granted to be associated with these structures. It would be only another step for such glands to be occluded and infected as glands in other surfaces of the body and thus set the stage for an infected pocket with an inadequate opening that flares up and gives symptoms from time to time.

Gilbert and Cintrón⁵ found none of their diverticula in nullipara. This was not a characteristic in our group of 15 cases. Nullipara showing this condition comprised 30 per cent of our cases. One half of the nullipara were married, the others were single. Perhaps these latter are more likely to be congenital in origin. It was noteworthy that all cases where diverticula were seen in nullipara, the openings were wide, almost equal in diameter to the underlying pouch and often bridged by a thin strand of tissue (fig. 3). These wide mouthed structures have less purulent material exuding from the openings, but tend to present bizarre symptoms such as hematuria, pains referred to the pelvis, loin or thigh rather than the frequency of urination and dysuria so typical of pure infection. Congenital diverticula are not frequently reported but are found in the literature from time to time.^{3, 6, 11, 12, 15}



FIG. 2. Diverticulum dissecting well posterior under trigone (oblique view)



FIG. 3. Multiple openings to multiple sacs beneath urethra

The embryology of the periurethral glands is so well described by Huffman.⁸ Even though the literature may have conflicting opinions expressed regarding the presence of these glands and their ducts, it seems logical that such structures do occur and often are responsible for the finding of such pockets communicating with the lumen of the urethra. The lining of the sac may be the factor that decides whether the diverticulum is congenital or acquired. The congenital diverticulum is likely to be lined with stratified squamous, cuboidal or transitional epithelium

while the acquired structure may have only thick granulation tissue as its lining. It is possible of course, for infection to destroy the epithelial lining but when it is found, the etiology is more likely to be congenital in origin.

Carcinoma has been reported in diverticulum of the female urethra.¹⁸ Infection with metaplasia of the lining membrane may have been the cause of this finding.

Because of the origin of the diverticulum from glands or cysts beneath or in the submucosa of the urethra, the sac may develop in one of two ways. First, it may dissect between the mucosa and muscular elements of the urethra and confine itself to the submucosal layer. Here the vascularity is marked for this is the corpus spongiosum of the female urethra. Second, the sac may herniate through the muscular fibers of the urethra. Thus it comes to be directly beneath the vaginal mucous membrane. The neck of the sac usually is well defined as is the sac, and dissection usually more simplified when treatment is carried out.

SYMPTOMS

Diverticulum of the female urethra is much more common than is generally suspected. The attention of the gynecologist is aroused by a mass presenting in the anterior vaginal wall and when pressure is applied to the mass, pus exudes from the urethral meatus. Vaginal pain, discharge and dyspareunia may be present. Such symptoms are not necessarily the ones that lead the urologist to be aware of this condition. Frequency of urination and dysuria are the common complaints of female patients and because of a lack of findings in the upper urinary tract, a diagnosis of chronic urethritis is often made. The diagnosis of urethral diverticulum is not difficult to make providing the condition is borne in mind. It is much like an ectopic ureter opening into the vestibule, it usually can be found where a thorough search is made when symptoms suggest such a structure. Moore¹³ states, "diagnosis of the lesion is not difficult if four important points are kept in mind; careful history, thorough physical examination, urethroscopic inspection and urethrography".

DIAGNOSIS

Concerning the diagnosis of lesions of the female urethra, it should be pointed out the symptoms of urethral diverticulum are similar to the symptoms of other diseases of the urinary tract. One must remember that careful and repeated search is necessary to detect the presence of such a structure and that, above all, recognition of a diverticulum usually is dependent upon the examiners recognition of the possibility of its presence. There is no doubt that visualization of the orifice may be very difficult. I have experienced occasions where at one examination nothing could be seen. At a subsequent study, the opening was evident, usually with purulent material escaping from it. While viewing the urethra with the pan-endoscope, intermittent opening and closing of the water inlet stop-cock, releases the pressure on the urethral floor and allows the contents of even small sacculations to escape into the field of vision and thus reveal their previously undiscovered hiding place.

Just as any complete urologic study includes a study of the pelvis, vagina and

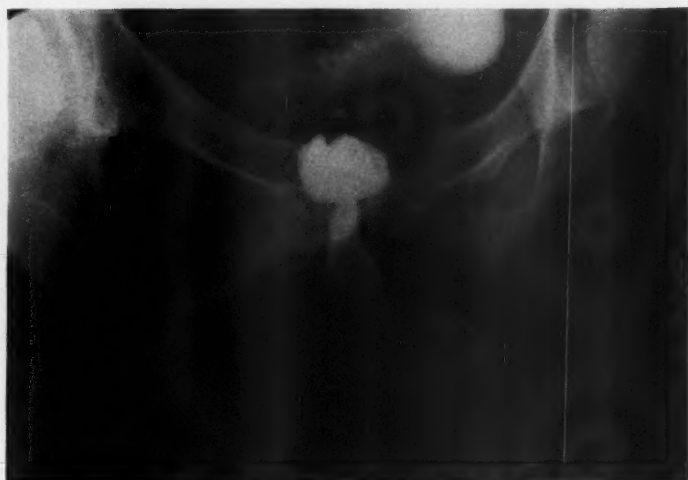


FIG. 4. Medium size sac beneath distal third of urethra

cervix, any examination of the urethra should include stripping it. Thus the diverticulum or its accompanying induration can be felt and its tell-tale contents expressed from the external urethral meatus.

When the orifice of the sac can be visualized, a ureteral catheter can be inserted and dye injected for visualization by roentgenogram. However, I prefer to carry out the urethrogram by injecting the opaque medium directly into the external urethral meatus by a blunt tip syringe. The sac usually fills and gives the surgeon a good picture of what the problem is when he comes to deal with it. I have used either 35 per cent Diodrast or a mixture of equal parts Lipiodol and sterile mineral oil (figs. 1 to 6).

The opening to a diverticulum may be extremely small. Taylor¹⁶ has suggested a method of filling the sac under pressure and visualizing it. He uses a Foley catheter the end within the bladder having been occluded by a strong silk tie. An opening is made in the catheter just distal to the retention balloon. After inserting and inflating the catheter, the balloon is drawn down tight against the bladder neck. All air is expelled from the catheter and urethra by filling them with the opaque medium. The external urethral meatus is occluded by means of an Allis clamp. The injection of the sac is thus accomplished by the pressure resulting within the urethra when the catheter is injected. Due to the necessity for a clamp on the external urethral meatus, anesthesia must be used. The large number of cases seen by him bespeaks for the efficiency of his methods of study.

Over a period of 10 years, 1945 to 1955 we have seen 15 cases of urethral diverticulum in the female. The ages of the patients varied from 25 to 56 years. The average age being 38 years. Thirteen were married; 11 had borne children; 2 had not; 2 were single. Dysuria was by far the most common symptom followed closely by lower abdominal pains and frequency of urination. Hematuria oc-



FIG. 5. Multilocular sac



FIG. 6. Sac with rather large capacity

curring at the end of urination was not uncommon. Dyspareunia, vaginal mass and interference with the urinary stream were seen less often. The symptoms usually were of short duration, a few weeks to 8 or 10 months. Only 2 patients showed symptoms lasting over a period of years. Those symptoms were of long standing unexplained frequency of urination. Eleven of the diverticula could be demonstrated by roentgenogram. Four patients had small openings that could be seen by endoscopic methods, but would not admit the dye when injected into the urethra.

TREATMENT

In general any patient having sufficient symptoms who has sought out the advice of a urologist, surgeon or gynecologist, will of necessity, have to have something done about the situation. Excision offers the best chance of complete relief. It is true the small cellulæ beneath the urethra that are discovered at the time of urethroscopy and are asymptomatic, do not need immediate attention. However, the patient should be warned of their potentiality and likely cause of trouble if and when they become infected. Those that are infected, are the ones that produce the symptoms. Various methods of attack have been described. All have to do with a method of facilitating dissection of the sac. If this is not done, recurrence is assured or a urethrovaginal fistula will result. Furniss⁴ suggested an incision into the sac through the anterior vaginal wall and electrocoagulation of the lining. The sac then was packed with gauze. If, and I would suppose it often did, a fistula developed, it was closed at a later date. Young¹⁹ suggested a sound be passed into the urethra and into the opening of the diverticulum. This aided in incising down on the sac and facilitated its dissection. Hunner⁹ had a similar method of recognizing the sac. After the sac was removed and the urethra closed, he advocated cutting away the redundant vaginal mucosa on only one side, thus forming a flap of the other. This flap was brought across the urethral repair, plicating it and resulting in two lines of sutures parallel but not one above the other.

Obviously if the sac can be packed with something to cause it to maintain its shape, dissection is much more simple. A sac filled with pus or urine will not maintain its shape on manipulation, when the orifice within the urethra is still patent. With the above idea in mind, Hyams and Hyams¹⁰ suggested packing the sac transurethrally with gauze or rib dam. I have tried this on several occasions early in my experience with this situation and found it very difficult. Cook and Pool² state that a small ureteral catheter inserted through the urethral ostium and coiled in the sac is a great aid to the surgeon.

I have found a combination of the methods suggested by Young¹⁹ and Hunner⁹ coupled with that described by Moore¹³ to be best in my hands. Moore uses a 16-F Foley catheter to outline the sac. The distal tip of the catheter is cut away as far as the balloon. A stab wound is made into the sac through the anterior vaginal wall and the catheter inserted through this opening. A purse string suture in the vaginal wall is placed around the catheter and the balloon is inflated to the proper size to outline the sac. An elliptical incision around the purse string is

made through the anterior vaginal wall permitting exposure of the sac wall. The distended Foley bag not only converts the diverticular sac into a semisolid tumor, but permits traction facilitating the dissection. Not all sacs are large enough to accommodate the Foley bag or easily recognized from the vaginal side to allow free incision before the sac is definitely identified. I have used a flexible probe point needle which is inserted into the urethra under vision using a pan-endoscope. The probe point is passed down into the sac through the urethra ostium. If the sac has been proved small by urethrogram, 10 per cent methylene blue is injected into the sac to stain its lining. The probe pointed needle then is used as a guide, as Young used a sound, to make the incision in the anterior vaginal wall. If the sac is large enough, the 16-F Foley catheter then can be inserted. If small, the lining of the sac can be recognized by the bluish discoloration of its wall.

When the sac is dissected free the urethra is closed with 2 rows of No. 0000 chromic catgut. The vaginal flap is placed so as to make sure the sutures are away from the urethral repair as suggested by Hunner. An indwelling Foley catheter which is placed in the bladder at the beginning of the operation, helps to identify the urethra and repair the defect. This catheter is left in place for 10 days. A vaginal pack is placed against the vaginal flap to obliterate any dead space. This packing is left in place for 48 hours. By this method, there have been only 2 urethral fistulas in 15 cases. Both were closed easily at a second operation.

SUMMARY

The importance of bringing before the clinician from time to time, the problem of urethral diverticulum in the female, is discussed showing a definite relationship to the finding of these cases to the times the situation is reviewed in an open meeting. The etiology, symptoms, diagnosis and methods of treatment are discussed. The virtues of the various methods of treatment are brought out and the method that has proved best in the author's experience is described. I would like to remind the reader that the frequency with which one finds diverticula of the urethra in the female depends on one's awareness that such a situation is likely to be present.

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VISUAL METHODS IN SURGICAL PRESENTATION

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We all have attended meetings at which fine papers were presented, yet for some reason failed to make the impression which the author intended. More often than not, failures of this nature result from poorly or unwisely prepared visual material. The old adage that "one picture is worth a thousand words" is unquestionably true. But pitfalls exist in that statement into which too often the unwary fall. Despite the truth of the saying, one should not conversely try to get a thousand words into one picture. This paper is not intended to cover all visual methods in surgical presentation, but the most common and widespread, namely the lantern slide. The motion picture is a subject within itself, which unfortunately cannot be covered within the scope of this paper.

Any discussion of lantern slides for scientific illustrations must be initiated by a comparison of the small, or 2 by 2 inch slide, and the large or standard $3\frac{1}{4}$ by 4 inch size slide. The use of the small or 2 by 2 inch size slide usually is predicated upon the use of 35 mm. film as a source, especially for color. There are several factors which militate in favor of the use of the smaller size; namely, weight, ease of storage, ease of transportation, low cost, low breakage, the consistent use of a uniform matte size and the relatively high quality color which can be obtained from the various 35 mm. film color emulsions. Those factors which deprecate the use of 2 by 2 inch slides are; the size, in that a very small area of projection surface is available, plus the relative restriction of choice of emulsion type and characteristics in 35 mm. film. In view of such limitations, these slides in general are not considered very satisfactory for the presentation of data.

It is impossible to do hand work upon these slides due to their minute size and the film emulsions available are of such a type that control in their processing is extremely critical. For good black and white work in the small size, extreme care is necessary.

In comparison, the larger so-called standard size lantern slide of $3\frac{1}{4}$ by 4 inches dimension, has the disadvantages of; increased bulk, increased weight, increased difficulty in transportation and increased storage space requirements. They are considerably more fragile because of the larger size of the glass plate involved. Their cost is greater than that of the smaller slide. However, in most respects the advantages of the larger slide far outweighs its disadvantages. Many emulsions of widely varying characteristics are available for use in production of the larger size slide which promotes better quality. The control of these emulsions in processing is much simpler since they are handled singly rather than in a continuous roll. Hand work may be done on these slides without difficulty when desirable.

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Presented during the Tucson Assembly of The Southwestern Surgical Congress, April 16-18, 1956, Tucson, Arizona.

The color emulsions in the larger film sizes are superb in their ability to faithfully reproduce the natural color of the original material and are gradually becoming less expensive. However, the cost of the larger color transparency is still high. It is evident that the larger slide is more practical for the average physician who is preparing a paper for a scientific meeting.

In regard to the actual technic of visual presentation of material, a few basic principles should be emphasized. First is the desirability of the use of a uniform matte size in preparing projection material. It is quite disturbing to an audience to have pictures of first one size and then another flashed upon the screen. This is equally annoying to the projectionist. He never knows whether or not slides will fill the screen or will overlap the edges. In the $3\frac{1}{4}$ by 4 inch slide, maximum projection area is available of about $2\frac{1}{2}$ by $3\frac{1}{4}$ inches.

The demonstration of data is more satisfactorily shown by what is popularly called a negative slide. The material appears as white letters or numbers on a black background. It will be remembered that in the old silent movies, legends and titles were nearly always made in this fashion. When a positive slide is projected, the screen is filled with a brilliant flash of white background material thereby producing a constriction of every iris within the audience, with the resultant unpleasant sensation of glare. The effect of diagrams, charts and graphs, and tables, is greatly enhanced when projection is by means of white on black, or negative slide technic. Of course, for the showing of half tone drawings, the slide must be positive to be visually acceptable.

In the actual presentation of a paper, visual material should be grouped as much as possible on the basis of type, as well as informational content. A good effect obviously would not be produced on an audience in which monochrome data slides are interspersed at random with color. It is more effective to plan the paper and its informational content to fit, within limits, around the visual material to be offered at the same time. This obviously promotes smoother continuity. Continuity is just as important in the presentation of this material as it is in the editing and cutting of a motion picture film.

Unless there is a specific reason for doing otherwise, numerical data should always be expressed in percentile figures. For example, all of us have encountered the paper in which the author stated that "out of 1,530 cases, 329 cases developed complications." Now these figures in themselves are relatively meaningless, whereas had the author stated that "out of 1,530 cases, 21 per cent developed complications," we would have had a much clearer understanding of the information the author was attempting to convey.

One of the most common errors encountered in illustrations shown at scientific meetings, is the tendency to place too much information on one slide. It must be remembered that a slide is only going to be displayed for a relatively short time and to be effective must forcefully and clearly show an easily assimilated informational content. Tables for publication often are too extensive to be appropriate slide material. In this case, the information should be digested for projection.

In respect to the mechanics of data presentation, graphs probably are the most common forms of communication used. Of the several types of graphs,

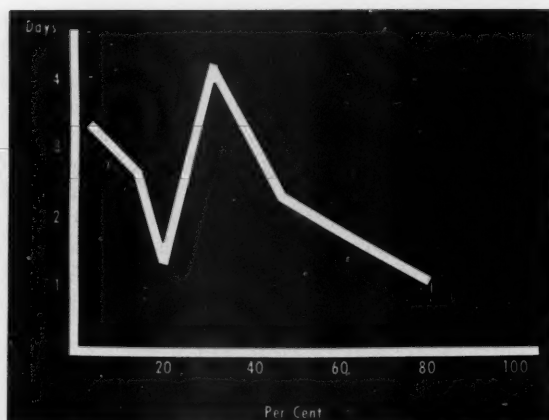


FIG. 1. Example of linear graph constructed with $\frac{1}{4}$ inch black adhesive Cellophane tape and numbered with a photo composing machine.

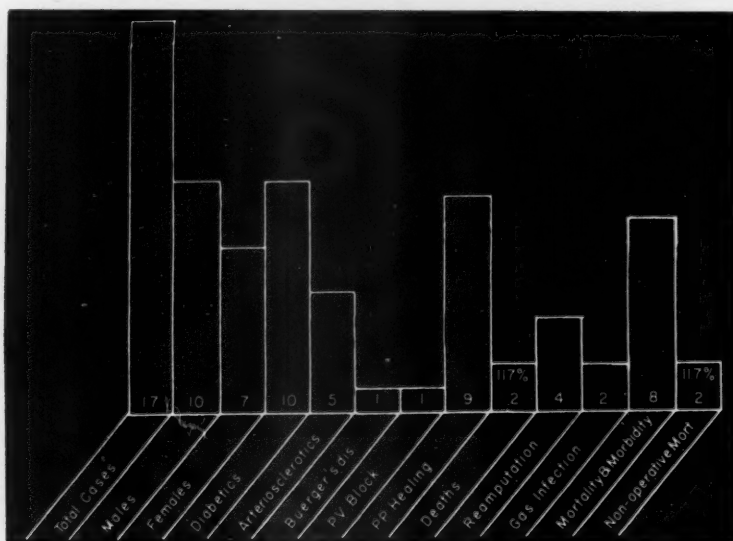


FIG. 2. Bar graph drawn in ink and lettered with a LEROY lettering machine

undoubtedly the linear graph, in which the progress of figures is charted against an ordinate and an abscissa, thereby visualizing two functions of the material in question, is the most widely used (fig. 1). Of all the methods of graphic presentation, probably the bar graph is one of the best (fig. 2). Information may be correlated and assimilated very rapidly by its use. It also has an advantage mechanically in that color may be added by the use of hand colors to the slide, thereby, producing a more impressive and eye-catching illustration. Circle or pie graphs occasionally are quite useful for similar reasons. The audience can grasp immedi-

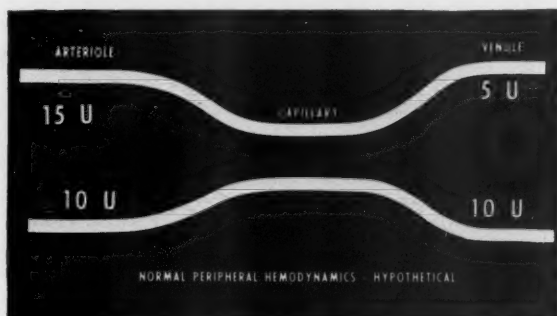


FIG. 3. Diagram constructed from black vinyl $\frac{1}{2}$ inch adhesive tape and lettered with photo composing machine.

ately all of the data. Of course, in the circle graph percentile presentations of quantities are required.

In pursuing the purely mechanical problems of preparation of material, all of us have encountered the situation in which no artist is available to prepare the material.

Such a situation exists at our hospital at the present time. All of the material shown in figures 1 and 3 here, were prepared without the aid of an artist. Since this paper is fundamentally a "how to do it" type, it is appropriate to discuss a few of the ways that have been found of circumventing the absence of an artist. Charts and graphs can be prepared very satisfactorily by the use of $\frac{1}{4}$ inch and $\frac{1}{2}$ inch black cellophane tape, applied to a suitable illustrators board. These tapes work very well when straight lines are desired. When lines must curve, by reason of the nature of the information it is desired to convey, vinyl "Scotch" brand, number 33 electricians insulating tape is quite satisfactory since this tape can be stretched and drawn into gentle curves. For linear graphs requiring the parallel presentation of several series of data, colored cellophane tapes are quite useful. These are available in a variety of colors and widths, and when photographed on either Ansacolor or Eastman Ektachrome reproduce quite well for projection.

Figure 1 is a sample graph which is constructed of the aforementioned $\frac{1}{4}$ inch black tape, figure 3 is a diagram which is constructed using the vinyl electrical tape which can be bent into gentle curves while being applied to the mounting board.

The next problem which arises is that of labeling and numbering these graphs which have been constructed. Several methods are available to do this without the assistance of a qualified artist. Probably the best and easiest is the use of a photo composing machine. Photo composing machines use fonts of type which are actually high contrast negatives, through which a sensitized material, usually paper, is exposed, producing the necessary lettering and numbering after appropriate processing. These then can be cut out with scissors and applied with rubber cement to the appropriate chart or graph in the correct position. Upon being photographed on high contrast type film, these "paste ups" can be repro-

duced in very good quality. The data examples which have been shown have all been labeled and numbered by this method as shown in figures 1 and 3.

Now these machines are somewhat expensive, for the use of any but relative large institutions. Many printing establishments which do offset printing employ these machines and will compose copy for a very small fee. However, there are available on the market printed adhesive-backed letters, two commercial types of which are known as Art-Type and Craft-Type. These may be obtained, cut out and pasted in the appropriate spot on a chart. A third method of labeling may be accomplished by the use of the LEROY lettering machine which is a mechanically guided pen which uses appropriate templates to control the size and style of the letters desired. The fourth method is that involving the use of a typewriter. If an ordinary typewriter is used, it is essential that the sheet be backed up with black carbon paper, the carbon facing the type rather than facing away. This intensifies the contrast of the printing. The other method which is often used, and is much more satisfactory, is the use of a composing machine comparable to the Vari-Typer. This is a composing machine which utilizes a large number of fonts so that the type style and size may be varied within reasonable limits. Due to the relatively small size of printed material available by these latter technics, they are appropriate primarily in the construction of tables rather than in the labeling of graphs.

Mention should be made of some of the emulsions which are available for the $3\frac{1}{4}$ by 4 inch slide size for the preparation of chart, graph and tabular slides. Either Ansco Reprolith or Eastman Kodalith film is ideal for this process. These are photo mechanical films with a very low shrinkage base and extremely high contrast. There is practically no gradation inherent in these emulsions when properly processed. It gives complete black and complete white with appropriate exposure and processing. If these films are unavailable, then one of the process types of orthochromatic films will do quite well, although they do not have quite as high a contrast as the aforementioned types. After processing, all of these films will be found to have tiny pin holes, or defects, within their emulsions which will allow spots of light to pass through. It is not difficult at all to spot these pin holes with a small camel hair brush and one of the various opaque media which are readily available commercially.

SUMMARY

In summary, the basic principals involved in presentation of visual data for scientific purposes are re-emphasized. The material should be presented in as simple a manner as possible. Numerical data should be presented in a uniform percentile manner. Care must be taken not to present too much information on a single slide. Color should be used wherever practicable, whether inherent in the film or added to the slide. The slides should be grouped as much as possible as regards to color and content. The use of a uniform matte size is extremely desirable and data slides are best presented by the negative technic.

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COMBINED INTESTINAL RESECTION AND PLICATION FOR TALC GRANULOMATOSIS

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The capacity of talcum powder to produce tissue granulomas has led to its abandonment, in recent years, as a surgical glove lubricating powder. This potential hazard of talcum powder was first recognized by Antopol¹ in 1933 and has been emphasized by numerous investigators since that time.^{2, 4, 7, 8} Although these observations have resulted in the replacement of talcum powder with more suitable materials, talc granulomas still may occur in persons whose contamination occurred prior to the disappearance of talcum powder from the operating room.

The purpose of this report is to present an unusual case of talc granulomatosis, with a prolonged history of recurrent intestinal obstruction, in which a profoundly virulent tissue reaction occurred 30 years after the suspected time of initial contamination. This patient was managed successfully by resection of the right colon and a significant portion of the distal small intestine followed by plication of the remaining small intestine and an end to end anastomosis between the small intestine and the transverse colon.

CASE REPORT

The patient, a 66 year old white businessman, was admitted to the Ball Memorial Hospital on March 18, 1954, because of abdominal pain, distention, nausea and vomiting of 20 hours' duration. The pain was intermittent and cramp-like. The vomitus had become increasingly fecal in appearance and odor.

The patient's past history of 30 years of frequent episodes of intestinal obstruction was of considerable interest. He had been operated upon in 1924 for acute appendicitis with perforation and generalized peritonitis. The appendix was removed and he was discharged from the hospital 23 days after operation. Seven days following his release from the hospital, he suffered the onset of his first attack of crampy abdominal pain, distention and vomiting.

Although these symptoms cleared shortly, he continued to be troubled with episodes of recurrent obstruction of varying degrees of severity. These episodes occurred every 1 to 3 months. The attacks were generally relieved, after several hours, by the violent vomiting which seemed to "jerk the kink out." In 1931, he was operated upon two times within a period of 30 days for intestinal obstruction. However, the character and frequency of the symptoms of obstruction remained essentially unchanged. Severe attacks of obstruction in 1949 and 1953 necessitated prolonged hospitalization with Miller-Abbott tube decompression and parenteral fluid and electrolyte maintenance.

The significant physical findings on examination were limited to the abdomen. There was considerable abdominal distention with generalized tenderness. The bowel sounds were high pitched and clearly obstructive in character. The laboratory studies which were carried out on admission showed evidence of dehydration. The red blood cell count was 5.2 million per cu. mm. and the hemoglobin was 16.5 grams. The urine specific gravity was 1.028. The white blood cell count was 13,500 with a smear differential of 83 per cent polymorpho-

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FIG. 1. Roentgenogram of the abdomen demonstrating small bowel obstruction

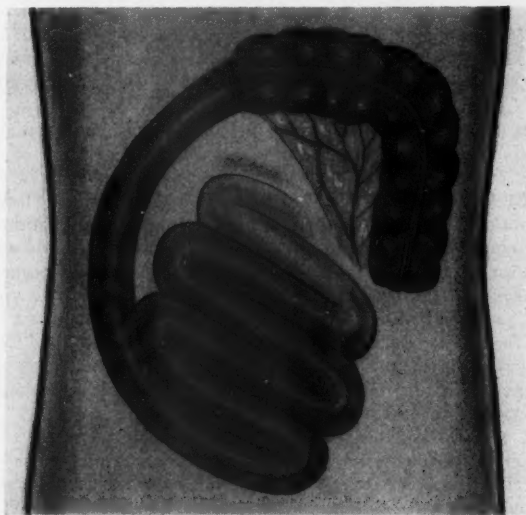


FIG. 2. Drawing of the plicated small intestine and the end to end anastomosis between the ileum and transverse colon as it appeared at the time of operation.

nuclear leukocytes, 16 of them being band forms. Flat roentgenograms of the abdomen revealed marked small intestinal distention with air and a step-ladder appearance of the loops of intestine (fig. 1).

The patient was taken to the operating room several hours after his admission to the hospital, following replacement of some of the lost fluid and electrolytes. The peritoneal

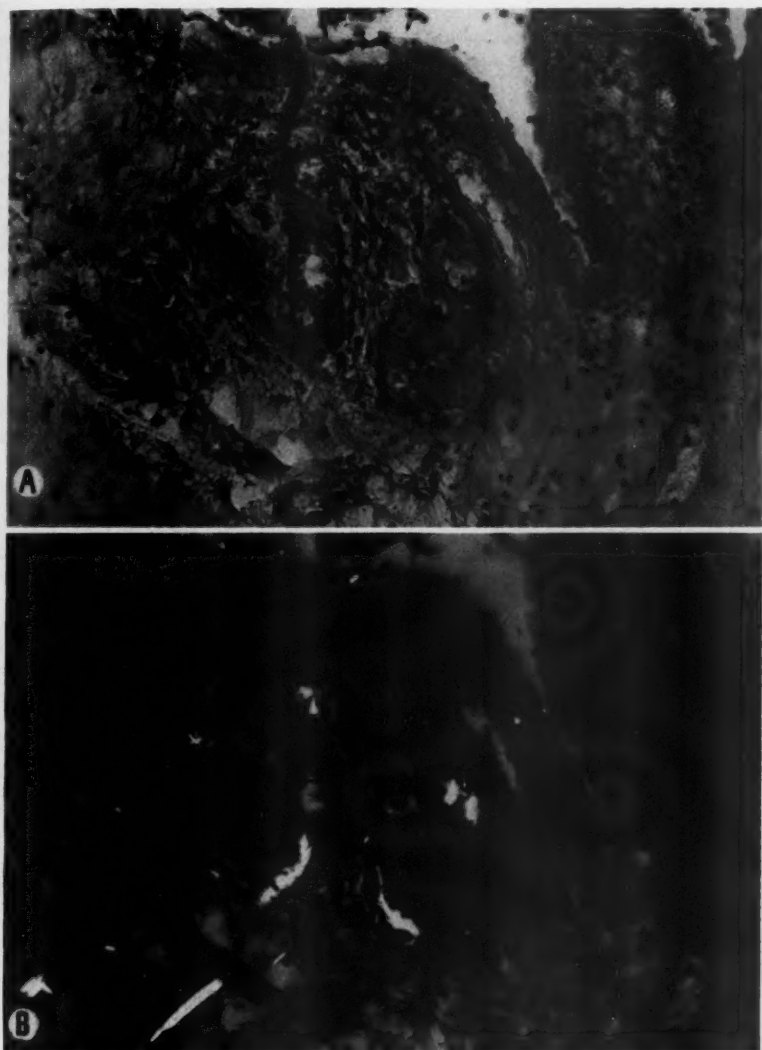


FIG. 3. Photomicrographs of one of the areas of talc granuloma in the wall of the small intestine showing (A) the proliferative type of foreign body reaction with standard lighting of the section and (B) the presence of birefringent talcum powder crystals in the granuloma with polarized light.

cavity was entered by means of a right rectus, muscle retracting incision. Marked distention of the small intestine with air and fluid was encountered. Numerous adhesions had matted and ensnared the middle and distal portions of the ileum. The adhesions were easily divided and the areas of obstruction relieved. All of the involved small intestine was completely freed up. Due to the marked distention of the small intestine, it was apparent that the incision could not be closed without the greatest amount of difficulty and without considerable tension being exerted on the tissues utilized in the closure. For this reason, a careful decompressive ileotomy was carried out. In addition to a large amount of air, 2000 cc. of fluid were aspirated from the distended small intestine, completely collapsing it. The incision was closed without difficulty. The postoperative course was uneventful and the patient was discharged from the hospital on March 29, 11 days following operation.

The patient had been home only 4 days when the symptoms of intestinal obstruction recurred. The presence of obstruction was confirmed by physical examination and roentgen study. Decompression was achieved and the obstruction was relieved by means of a Miller-Abbott tube. He was discharged from the hospital 7 days later, on April 9.

Because of the long history of recurrent intestinal obstruction and the prompt failure of lysis of adhesions only, plication of the intestines was decided upon. When the patient had recovered sufficiently he was readmitted to the hospital on April 20 and was operated upon the following day.

The small intestine, especially its more distal portion, was densely adherent to itself and to the abdominal wall. The adhesions were most unusual. They were quite dense and firm. It was virtually impossible to divide them. It was as though the bowel had been immersed in concrete which had been permitted to harden. There appeared to be little likelihood that the small intestine could be dissected free of this rigid matrix. After several false starts and several inadvertent holes in the small intestine, efforts in this direction were abandoned as futile. The right colon, which was involved in this process, was resected with approximately 30 per cent of the small intestine. Although the proximal portions of small intestine had been found to be free of adhesions at the March 18 operation, filmy adhesions were found to extend up to the ligament of Treitz. These were quite easily divided. The small intestine was plicated from the ligament of Treitz down to the point of resection. An end to end anastomosis was carried out between the divided end of the small intestine and the transverse colon (fig. 2). The incision was closed in layers with sutures of fine silk.

Microscopic study of the resected intestine and associated matrix revealed considerable chronic inflammation with numerous foci of giant cells. Through the use of polarized light, the giant cells were found to contain doubly refractile bodies characteristic of talc granulomas (fig. 3).

Gastric suction and parenteral administration of fluids and electrolytes were maintained until the return of good bowel sounds. The postoperative course was relatively uneventful. He was discharged from the hospital on May 8. In the 2 years since operation, he has been completely free of abdominal distention and pain. He has not noticed the slightest tendency toward recurrence of the old disabilities which had plagued him so frequently for 30 years. The consistency of his stools ranged from loose to semisolid for the first 18 months after operation. In the past 6 months they have become increasingly more solid.

DISCUSSION

The delayed massive activation of the talc granulomatosis process was the most striking clinical feature of this case. It was as though one had stirred up a "hornet's nest" of the most undesirable type of tissue reaction. Because of the exceptionally rigid and unyielding nature of the enveloping adhesive matrix, efforts to free up the distal small intestine from this congealed mass were completely ineffectual and resection became clearly the only possible course of action. Plication of the remaining small intestines was carried out, following the division

of filmy adhesions, because of the earlier failure of lysis of adhesions alone. The patient's marked symptomatic relief from frequently recurring episodes of intestinal obstruction during the 2 years since operation has been most gratifying.

The findings in this case fulfilled the criteria for the diagnosis of talc granuloma suggested by Eiseman, Seelig and Womack² in 1947. Multiple areas of the proliferative type of foreign body reaction with multinucleated giant cells and fibrosis were identified. The reaction was found in the area of previous operative procedures and the clinical history was characteristically a long one of chronic disability. Talc crystals were identified within the granulomas through the use of polarized light. This ability of talc crystals to rotate a beam of polarized light was first employed in the study of talc granulomas by Fienberg³ in 1937.

The dense, stenosing type of fibrosis produced by talc has been emphasized by many authors. In a few patients, a significant latent period has occurred between the original operation and the onset of symptoms. Gruenfeld⁵ encountered an interval of 11 years between talc contamination and the appearance of a large abdominal granulomatous tumor in one patient. Intervals of approximately 10 years were reported in 2 of the patients of Eiseman and his associates.

It is of interest to consider the possible activating role of both infection and trauma in the production of the talc granuloma. Both have been suggested as possible stimulants to the production of these granulomas by some authors. Infection, in the form of appendiceal perforation and generalized peritonitis, was an important feature of the illness of my patient at the time of his original operation. Through the mechanism of dividing adhesions in this patient, the suggested potentiality of trauma to stimulate profound tissue reaction was dramatically illustrated. Animal experiments carried out by Saxen and Tuovinen¹¹ in 1948 and by Johnson⁶ in 1953 suggest that tissue trauma plays a part in the development of talc granulomas.

Sinus formation, principally abdominal, was the most frequently encountered complaint in the 37 patients whose cases were reported by Eiseman and his associates. It was found in 18 patients. Intestinal obstruction occurred in 7, fecal fistula in 5 and a tumor mass in 3 patients. Bowel resection was required in 7 of their patients. Intestinal plication was not employed by them. The author has been unable to discover any reported experience with the combined use of intestinal resection and plication for talc granulomatosis.

Although my personal experience with intestinal plication in a rather limited number of patients is far from satisfying, the experience in this patient suggests that, if ever there is justification for plication, a situation such as the one here must be it. In this regard, the author wishes to emphasize that he views the widespread use of intestinal plication^{9, 10} with considerable misgiving and believes that clear indication for its use may only rarely be encountered.

SUMMARY

A case of massive activation of talc granulomatosis in a 66 year old man, producing intestinal obstruction, is reported. The activation was precipitated by lysis of adhesions for intestinal obstruction and occurred 30 years after the

presumed initial talcum powder contamination during appendectomy for acute appendicitis with perforation. The patient had suffered from frequently recurring episodes of cramp-like abdominal pain and intestinal obstruction during the 30 year period. He was managed by resection of the right colon and approximately 30 per cent of the distal small intestine with plication of the remaining small intestine. An end to end anastomosis was carried out between the small intestine and the transverse colon. During a two year period of observation following operation, he has remained free of abdominal pain and has experienced no recurrence of intestinal obstruction.

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EDITORIAL

A GRADED APPROACH TO SURGICAL TREATMENT

Surgeons often must choose between a simple operation that is relatively safe and one which is more extensive and carries a higher mortality and morbidity. Often the more extensive operation is more effective in controlling the disease, but the question is whether its greater effectiveness outweighs the mortality and morbidity that are involved.

In many cases the decision between the two operations must be final, for the performance of the smaller one may make it impossible subsequently to perform the larger. An example of this is an incomplete removal of a thyroid nodule which later proves to be cancer and implants itself in the incision. But in other diseases there is a place for a graded attack. The selection of the initial operation for duodenal ulcer is an example.

Resection of two thirds or more of the stomach combined with vagotomy is probably the most effective operation for controlling the ulcer diathesis. The mortality rate after this operation is not excessively high and irreversible side effects are not common. Yet any operation that involves closing or anastomosing an inflamed duodenal stump carries a mortality rate several times as high as pyloroplasty or gastroenterostomy, and any operation that sacrifices a large part of the stomach is more apt to be followed by irreversible side effects than one which does not sacrifice the stomach.

The most serious sequela that is apt to occur after vagotomy with pyloroplasty or gastroenterostomy is recurrence of the ulcer. Recurrence, however, is correctible by a second operation, whereas the complications of extensive resections may not be correctible. Thus, although vagotomy with gastroenterostomy or pyloroplasty is followed by a higher incidence of recurrent ulceration, it is so safe and so free of irreversible complications that it deserves serious consideration as the first step in a graded attack on duodenal ulcer. It can be viewed as a therapeutic trial which if successful will avoid the dangers of resection.

The same principles apply to the treatment of a high-lying gastric ulcer. Resection of such an ulcer, with three fourths or more of the stomach, invariably cures the ulcer but does so at considerable risk of inducing permanent side effects. In such a case an alternative to resection of the ulcer and most of the stomach is resection of the antrum, leaving the ulcer in place. In the face of biopsies that show no evidence of cancer the risk of leaving a cancer is small and there is a good probability that resection of the antrum will cure the ulcer and leave the patient well. If the ulcer persists a more radical resection always can be done.

All through surgery the principle of the graded approach can be used. In large hernias it may be wiser to try simple repair with steel wire before resorting to operations, like implantations of mesh or transplantation of fascia, that carry a higher risk of morbidity. When there are multiple cysts of a breast, aspiration of the cysts can be tried before resection of the breast is considered. In small, asymptomatic multinodular goiters treatment with desiccated thyroid may

control the tendency to enlarge and obviate the necessity of subtotal thyroidectomy. A therapeutic trial of simple measures which are often but not always effective may avoid the morbidity of a major operation. If the therapeutic trial fails the major operation still can be done.

Even in the treatment of cancer there may be a place for a graded approach. Most surgeons treat cancer of the lip by wide local excision and reserve dissections of the neck for those patients in whom metastases are present or later appear. Melanomas often are treated in the same way. There is no statistical proof that prophylactic resection of regional nodes is any more likely to control the cancer than is therapeutic resection done soon after regional metastases are palpable.

In many cases when cancers give no evidence of having spread, resection or destruction of the primary tumor is an acceptable initial attack. A papillary cancer of the thyroid without palpable involved nodes is an example of a cancer which is well adapted to this approach. Low-lying rectal cancers that seem limited to the mucosa or are quite small can be treated successfully by electrocoagulation. Later, if they are not controlled, a combined abdominoperineal resection still can be done. Small cancers of the tongue and gingival margins, cancer in situ of the cervix and stage I cancers of the breast without palpable nodes, are all well adapted to local eradication, to accurate follow-up, and hence to a graded type of treatment. Careful evaluation of the results of such treatment may in the future enable us in selected cases to avoid much of the mortality and morbidity of extensive operations, indiscriminately applied.

When a limited operation has a good chance of controlling a disease and when performance of the limited operation does not jeopardize the success of a subsequent more extensive one, it may be best to try the simpler operation first.

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BOOKS RECEIVED

Books received are acknowledged in this section, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

Chemosurgery in Cancer, Gangrene and Infections. By FREDERIC E. MOHS, B.Sc., M.D., Charles C Thomas, Publisher, Springfield, Illinois.

Urology and Industry. By LEONARD PAUL WERSHUB, M.D., Charles C Thomas, Publisher, Springfield, Illinois.

The Initial Management of Thoracic and Thoraco-Abdominal Trauma. By LAWRENCE M. SHEFTS, M.D., HAROLD DODD, M.D., AND FRANK B. COCKETT, M.D., Charles C Thomas, Publisher, Springfield, Illinois.

Observations on Krebiozen in the Management of Cancer By A. C. IVY, Ph.D., M.D., JOHN F. PICK, M.D., AND W. F. P. PHILLIPS, M.D., H. Regnery Company, Publisher, Chicago, Illinois.



